BMEG 457 – Design History File (DHF) 10.

April 11, 2025

Client: Siemens Healthcare Ltd. (Siemens Healthineers Canada)

Project: Magnetic Resonance Imaging (MRI)-Based Pseudo Computed Tomography (pCT) Generation Using Ultrashort Echo Time (UTE) Technique

Team #17: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen

Faculty Supervisor: Tim Salcudean

Report Type: Final Report

Word Count: 56339

Abstract

The following document succinctly summarizes the Capstone Project for conversion of UTE-MR to pseudo-CT images for improved visualization of cortical bone. Further, the report compiles all relevant documentation throughout the course, referencing them as and when needed.

MI. *Master Table of Contents*

MII. *List of Tables & Figures (For DHF10 Only)*

M1. Summary Report

M1.1. Objectives

An Ultrashort Echo Time (UTE) MR to pseudo-CT (pCT) conversion prototype was developed in response to specific needs identified through extensive literature review and direct engagement with stakeholders at Siemens Healthineers, namely Dr. Lumeng Cui, Dr. Gerald Moran, and Dr. Stefan Sommer. Key objectives included improved bone-air and bone-soft tissue segmentation, performance across various tissue types, and support for accurate clinical diagnosis. Broadly, this initiative also sought to evaluate the feasibility of integrating pCT generated from UTE MR into clinical workflows, with the goal of alleviating long patient wait-times in the medical imaging sector. The core value proposition of the device is that it provides radiologists with high-quality diagnostic insights without the need for additional operational resources, thus reducing both time and financial costs for healthcare institutions.

In addition to implementing core processing functions such as bias-field correction, inverse logarithmic scaling, histogram-based thresholding, and segmentation across bone-air and bone-soft tissue interfaces, evaluation metrics and thresholds were established based on secondary research. These quantitative parameters formed the foundation for our design requirements and subsequent development of satisfaction curves. Key performance indicators included spatial resolution, geometric fidelity, and peak signal-to-noise ratio (PSNR), each weighted according to their clinical relevance. These factors informed the construction of a value equation to facilitate comparative analysis of future design alternatives for our imaging pipeline.

Kindly refer to *DHF #1* and *DHF #2* in the Appendix for further details.

M1.2. Design Process

Following exploration of our evaluation criteria and through regular consultations with our client, a Function Structure Diagram (FSD) was constructed to accurately capture the primary components of our potential solution. The workflow begins with capture of the MR images via a configured scanning system that implements a specialized Ultrashort Echo Time (UTE) with short-T2 sequences to highlight bone contrast. Next, our prototype performs preprocessing on the acquired images to correct contrast levels utilizing bias correction and inverse logarithmic scaling, followed by thresholding of anatomical structures using histogram peaks. This is proceeded by segmentation, where cortical bone is first distinguished from air and then later, from soft tissue. Deep-learning based methods could then be applied to enhance our segmentation performance. While deep learning approaches were explored to augment separation of anatomical structures, limitations in time and data volume precluded full model development. However, future iterations of the image processing prototype will incorporate machine learning components to allow for more accurate and generalizable segmentation results.

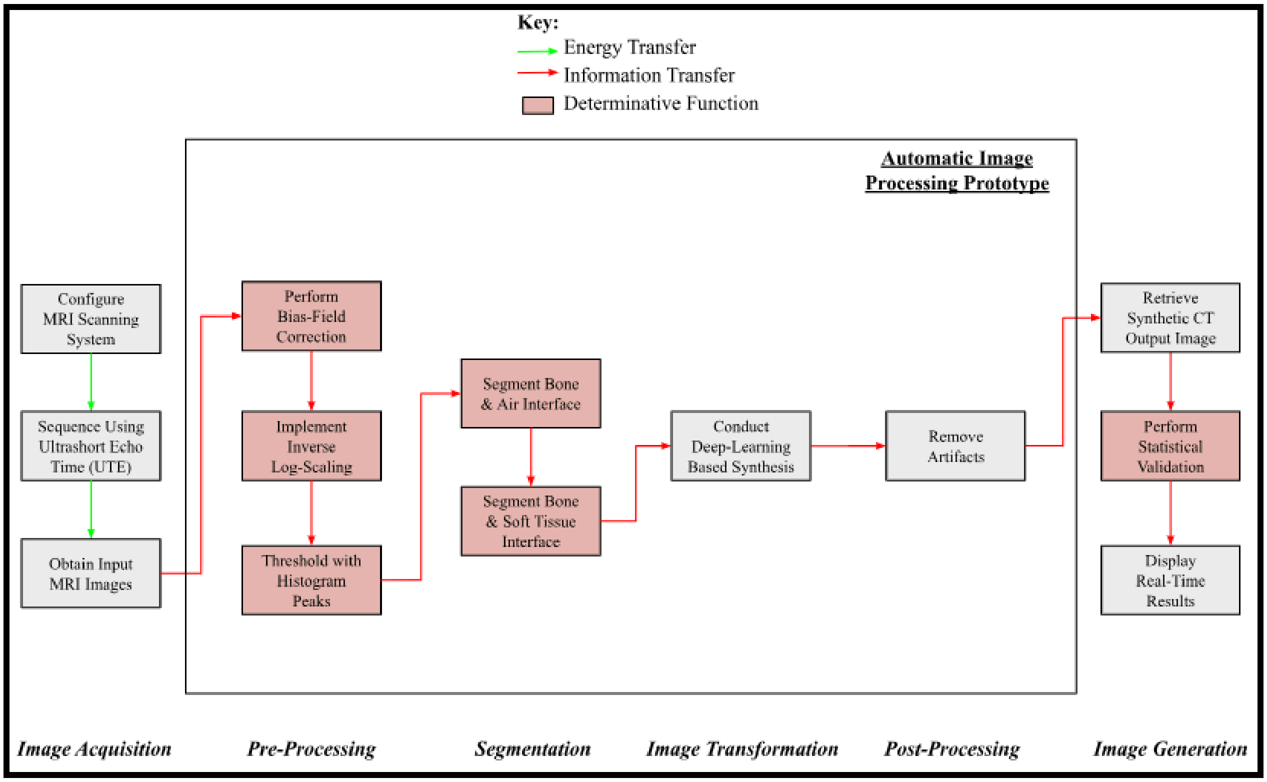


Figure M1*. Function Structure Diagram of the Proposed Workflow.*

Following identification of core functional requirements as captured by the FSD, our team developed a Critical Function Prototype (CFP) that formed the technical basis of the project for the remainder of the term. This proof-of-concept was presented to our academic supervisor, Prof. Tim Salcudean, TA Katie Chen, as well as our client, Dr. Lumeng Cui. The initial design demonstrated key foundational capabilities, through integration of inverse logarithmic scaling, bias correction, and segmentation for both bone-air and bone-soft tissue interfaces. These functionalities were retained throughout the project and served as the baseline for subsequent optimization, guided by empirical performance data and qualitative evaluations.

Please consult *DHF #3* in the Appendix for details on the FSD and exploratory research.

With regards to prototype optimization, our group built upon the CFP using histogram-based bias correction as directed by the client, in parallel with efforts to generate automatic thresholding for segmentation purposes. In the previous iteration of our workflow, we manually inputted the threshold values to perform segmentation. However, subsequent iterations incorporated automatic thresholding to facilitate a streamlined procedure with minimal human interference. Additionally, the team also focused on N4ITK hyperparameter optimization in order to improve the accuracy and effectiveness of the prototyping for bias-field correction. Combinations of the hyperparameters, SetSplineOrder, SetConvergenceThreshold, SetNumberOfHistogramBins and SetMaximumNumberOfIterations, were systematically evaluated across their full numeric range to yield the most optimal results. The aforementioned optimizations coalesced into our Alpha Design Review, which was presented to our Capstone Supervisor, Prof. Tim Salcudean, and client, Dr. Lumeng Cui, for their perusal and evaluation.

Kindly refer to *DHF #5* in the Appendix for our technical analysis and optimization.

As part of our iterative design approach, we also conducted a Fault Tree Analysis (FTA) to assess potential failure modes. A comprehensive diagram was created to identify critical failure points, along with tailored mitigation strategies, which informed several design revisions and updates to our system specifications. Furthermore, environmental impacts of our prototype were quantified via a Life Cycle Assessment (LCA), spanning manufacturing, operation, and disposal stages. The impacts for each process was comprehensively evaluated, comparatively ranked, and categorized by controllability. Finally, the energy consumption for the standard imaging pipeline, a potential deep learning add-on to the concurrent workflow, and a standalone traditional CT scan were computed to holistically assess the ecological footprint of our solution.

Please consult *DHF #6* in the Appendix for the FTA and LCA.

Upon completion of the Alpha Design, a NASA-Task Load Index was administered by our client, Dr. Lumeng Cui, to gather qualitative and quantitative feedback. The survey evaluated the usability and workload implications of our image processing prototype, confirming that the system placed minimal cognitive and physical demands on potential users. These positive outcomes supported the potential for seamless clinical integration. Lastly, design verification procedures were then conducted to confirm alignment with original specifications and evaluation criteria. This guided our next steps for our final design before project handoff to the client.

Kindly review *DHF #9* in the Appendix for verification and validation results.

Additionally, we were honored to present our prototype at the APSC Design & Innovation Day 2025, where our group showcased the key deliverables of the project after receiving permission from our client, Dr. Lumeng Cui. These included an abstract summarizing our work for a general audience, visual comparisons of MR inputs, pseudo-CT outputs, and gold-standard CT scans, as well as a code repository illustrating the operability of our software. Our poster presentation highlighted the motivation behind addressing this challenge in healthcare, detailed our imaging prototype, and emphasized its potential clinical impact. A formal invitation was extended to the client and his team in recognition of their consistent support, dedication and collaboration during the term, especially during the prototyping phase.

Please refer to *Design & Innovation Day Deliverables* in the Appendix.

M1.3. Design & Testing

The finalized solution is an image processing pipeline designed to synthesize CT-like images from UTE MRI data. This workflow addresses key challenges inherent in CT imaging, including intensity inhomogeneities, suboptimal bone contrast, and poor bone-air discrimination. The resulting synthetic CT images aim to improve anatomical fidelity while retaining the superior soft tissue contrast offered by MRI and exposing patients to no ionizing radiation. Thus, the workflow integrates the strengths of both imaging modalities for enhanced clinical utility. Below is a brief summary of the different image processing modules within our design (*Table X*).

Table M1. *Summary of Components of Image Processing Pipeline*

Step	Function	Components
Bias Correction	Corrects intensity inhomogeneities, improves soft-tissue contrast and reduces artifacts.	N4ITK with hyperparameter optimization, OpenCV,
Inverse Logarithmic Scaling	Significantly enhances the contrast of the bone signal.	Numpy (Inverse logarithmic function)
Histogram Analysis	Identifies and visualizes the signal peaks.	Numpy (Histogram calculation)
Gaussian Fitting	Fits Gaussian curves to the histogram for accurate thresholding.	Gaussian Mixture Model (GMM)
Automatic Thresholding	Automatically identifies threshold from the corresponding histogram.	Scipy (FWHM calculation)
Segmentation	Classifies pixel intensities into different regions such as bone, air and soft-tissue, based on the identified thresholds.	OpenCV (morphological operations)

User validation feedback from Dr. Lumeng Cui indicated that the system imposed minimal physical, mental, and temporal workload, with low frustration. Additionally, the prototype was deemed effective for the intended MR-to-pCT conversion task. These findings support the conclusion that the workflow can be readily integrated into clinical practice without introducing strain. However, future evaluations should involve a broader, less technically specialized user base, such as radiologists, with a larger sample size to cement results and ensure validity of the workflow's usability/adaptability within clinical settings.

Meanwhile, objective verification metrics including Dice Similarity Coefficient (DSC), Structural Similarity Index Measure (SSIM), and PSNR, yielded suboptimal values. This discrepancy likely stems from inherent differences in resolution and physical properties between MRI and CT imaging modalities. As such, it may be inappropriate to analyze these metrics solely based on paired-image assumptions. Thus, better quantifiable approaches are needed to allow for clinical interpretability and to guide subsequent steps for integration with refinement.

Please see *DHF #9* in the Appendix for a comprehensive discussion of these results.

M1.4. Conclusion

We believe this software workflow demonstrates strong potential for pseudo-CT as a viable alternative to conventional CT, offering enhanced MRI-based cortical bone imaging while minimizing radiation exposure. The successful implementation of key image processing steps such as bias correction, inverse logarithmic scaling, and automated segmentation, alongside favorable user feedback underscores the clinical promise of our approach. However, to fully realize this potential, further development is required, including quantitative performance enhancement, deep learning integration, and validation through rigorous clinical trials with a broader end-user base. With continued refinement, this workflow could significantly streamline diagnostic imaging and reduce reliance on traditional CT in clinical practice.

M1.5. Recommendations

To build upon the proof-of-concept established by the current software workflow, we recommend several focused next steps. First, the current pipeline's reliance on isolated 2D MR slices limits its throughput and clinical scalability; future iterations should prioritize full-volume processing capabilities. Second, deep learning approaches previously outlined in *DHF #3* should be integrated to enhance segmentation accuracy and automate complex image interpretation tasks. Lastly, clinical viability remains unverified in real-world settings. We strongly advise conducting formal evaluations with practicing radiologists to assess integration into existing imaging workflows and to validate usability and diagnostic efficacy. These steps are essential for translating the prototype into a deployable clinical solution.

M2. Appendices

M2.1. Design History Files

For this section, each DHF from 1-9 is presented below.

BMEG 457 – Design History File (DHF) 1.

December 06, 2024

Client: Siemens Healthcare Ltd. (Siemens Healthineers Canada)

Project: Magnetic Resonance Imaging (MRI)-Based Pseudo Computed Tomography (pCT) Generation Using Ultrashort Echo Time (UTE) Technique

Team #17: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen

Faculty Supervisor: Tim Salcudean

THE UNIVERSITY OF BRITISH COLUMBIA

Report Type: Capstone Project Proposal

Section Word Count: 5361

Abstract

The following project proposal summarizes the challenges involved in the implementation of Magnetic Resonance (MR) imaging for radiation treatment planning. Additionally, the proposal defines the problem scope, enlists stakeholders, specifies needs, and outlines a project roadmap.

II. *Table of Contents*

III. List of Tables & Figures

IV. Purpose

This proposal is prepared for Lumeng Cui, an MR collaboration scientist working for Siemens Healthineers, Canada. The following document has been prepared to address the potential use of MR as a substitution for CT in certain clinical scenarios. The proposal defines the problem scope, key stakeholders, existing alternatives, requirements and evaluation criteria for any proposed solutions, as well as a work plan that outlines the project timeline over the next 6 months. In summary, the document aims to dissect the biomedical problem and lay out any subsequent steps for the ideation, development and validation phases of the design process.

V. Executive Summary

The proposed image processing prototype for generating pCT images from UTE MR images focuses on addressing specific needs which have been identified from conducting rigorous literature research and through frequent client interactions. Some of these needs are as follows: improved bone-air segmentation, bone-soft tissue interface, performance on different tissue types, and accurate clinical diagnosis. Some of the primary stakeholders for this project are identified to be Siemens Healthineers R&D Team, radiologists, patients, and Siemens Licensors and Distributors. The perspectives of the aforementioned individuals helped the group to formulate our key needs and to align them with strategic specifications for the project.

The particular requirements for the design process focus on aspects such as spatial similarity, resolution, intensity distribution, image quality, and bone-air interface segmentation. Specific metrics and thresholds were identified from our secondary research, as well as other alternative solutions present in the imaging market. These requirements were expanded upon for the development of satisfaction curves from their corresponding evaluation criteria, some of which include spatial resolution, geometric fidelity, and peak signal-to-noise ratio (PSNR). Each criterion was assigned weights based on their overall significance and followed by formulation of a value equation for ranking proposed solutions in the future. A Gantt chart is provided which explicates the timeline for major deliverables as well as a roadmap underpinning key aspects of the project. Lastly, the resources required and the budget for the project is tabulated and summarized within the proposal.

1. Problem Scope

The following section characterizes the biomedical problem, outlines the different stakeholders involved, and provides a summary of alternative imaging solutions.

1.1. Biomedical Problem Definition

Magnetic resonance imaging (MRI) and computed tomography (CT) are two medical imaging modalities commonly used in the healthcare sector. Both of these have advantages and disadvantages, which make them suitable for different medical applications (*see Table 1*).

Table 1. *Advantages of MR and CT Imaging Modalities.*

Magnetic Resonance Imaging (MRI)	Computed Tomography (CT)
• Superior soft tissue contrast • No ionizing radiation • High sensitivity	• Superior imaging of bony structures • Bone and air differentiation • Electron density information for radiation therapy

In particular, these imaging techniques have proven to be of extreme importance in the diagnosis and prognosis of cancer patients. One specific pathway of treatment highly dependent on these imaging modalities is radiation therapy (RT), which uses high doses of radiation to treat cancer and can be used in conjunction with other forms of therapeutics [1]. This particular pathway for treatment is quite common, being prescribed to almost 50% of all cancer patients [2]. While all demographics can be affected by cancer, the majority of patients are above the age of 50 [3].

An important component of RT involves localizing the tumor and calculating radiation doses to minimize incident exposure to healthy tissues and organs. Damage to surrounding healthy cells can result in adverse side effects including hair loss, fertility problems, fatigue, nausea, and changes to the skin [4]. While CT imaging is the current standard for delineating the tumor and dosage calculation, limitations persist. The poor soft-tissue visualization of CT imaging can create difficulties in delineating tumors in regions surrounded by soft-tissue like the brain, prostate, pelvis, lungs, head, and neck [5].

Due to MRI's superior soft-tissue visualization, it has been investigated as a possible alternative to CT imaging. Despite the potential outlined in many research papers, the implementation of MR-only radiation therapy has not yet replaced the current standard. This is primarily due to the inability of MRI to provide electron density information needed for dosage calculation. Pseudo-CT images have been created from MRI to address this prominent shortfall. However, issues remain due to the poor bone visualization observed in MRI [6]. One technique, known as ultrashort echo time (UTE) MR has shown promise [6]. This approach uses short echo-times to capture signals from cortical bone before they eventually decay.

UTE-MR generated pseudo-CT could be a promising tool for RT. With its newfound potential to better mimic CT contrast, further testing and investigation of algorithms and models are needed to effectively develop this tool for implementation in a clinical setting.

1.2. Stakeholder Investigation

An analysis was conducted to identify the stakeholders affected by the defined biomedical problem. For each such individual or group, a series of justifications, needs, and critical questions were established *(Appendix 1-A, Table 1)*. A few of our key stakeholders are listed below:

- *Siemens Healthineers R&D Team:* This stakeholder is our client who is providing direct funding, access to proprietary datasets, and technical expertise.

- *Radiologists:* This stakeholder will be responsible for analyzing and interpreting images obtained from the product.

- *Patients:* The product will diagnose and evaluate patients, directly affecting this stakeholder.

- *Siemens Healthineers Licensors and Distributors:* This stakeholder will be impacted by conflicts relating to intellectual property, product quality, and use of Siemens' assets.

1.3. Identifying Alternative Solutions

We conducted a thorough literature search to find major alternative solutions that are currently available for the conversion of UTE MRI images to pseudo-CT images. All such solutions identified consisted of major techniques and algorithms that have been significantly tested with extensive data to support their outcomes. For a simpler evaluation of the alternatives, the strengths and weaknesses of each option were documented and contextualized with relevance to the project. Highlighting these pros and cons helped the group understand the shortcomings of current state-of-the-art technologies while recognizing possible areas of improvement. The table below summarizes key findings (*see Table 2).* For a complete list of our alternative solutions, see the enclosed document (*Appendix 1-B)*.

Table 2. *Summarized List of Alternative Solutions.*

Solution	Strengths	Weaknesses
Zero Echo Time (ZTE) MRI [7]	- Efficient capturing of short T2 bone signals - Excellent contrast between air, bone, and soft tissue - Strong linear correlation to CT images - Robust to motion artifacts	- Requires bias-field correction and inverse logarithmic scaling - Plastic signals from the RF coil are visible in captured images - Off-resonance blurring is possible at various tissue interfaces
Synthetic CT using Deep Learning [8]	- Higher accuracy than atlas-based approach - Generates sCT images rapidly, within 9 seconds per patient - Does not require manual segmentation - Utilizes transfer learning so that high accuracy is possible even with limited amounts of data	- Extended training period needed - Requires large volumes of data - Dependent on image alignment - Requires histogram matching and other pre-processing techniques
Synthetic CT using Multi Cycle GAN (Generative Adversarial Networks) [9]	- Performs better than cycle-GAN with smaller values for mean average error (MAE) and mean error (ME) - Requires fewer epochs (100) for training the model compared to cycle-GAN (150) - Detailed structures of the generated synthetic CT images are retained	- Requires a long training time of 140 hours to train the model
Pseudo-CT using Patch Based Generation [10,11]	- Eliminates the need for image registration - Visual and quantitative analysis depicts a high similarity between CT and pseudo-CT - Requires a GPU computation time of less than 9 minutes	- Requires MRI and CT images to be aligned accurately in the same spatial origin - Produces low resolution pCT images due to feature extraction - Generates large values of MAE due to underestimation of bony structures

1.4. Value Proposition

Implementation of pseudo-CT generated from UTE-MR images in the clinical setting can improve workflow, patient safety, and efficiency. While this product has a broad application, certain diseases would benefit greatly from its implementation, specifically cancer of the lung pancreas, liver, head and neck, prostate, and brain [12]. With more than half of people diagnosed with cancer needing RT at some point in their care, the demographic that will be affected by this product will be extensive [2]. It is estimated that MR imaging for simulation purposes is done in 24% to 32% of patients treated with RT. Similar projections can also be made for MR-only RT [13]. MR-only RT could allow for lessened side-effects for patients, more accurate diagnoses, and improved workflow for radiologists and physicians. This value proposition is summarized in terms of the gains created by the solution and possible pain-points alleviated (*see Figure 1*).

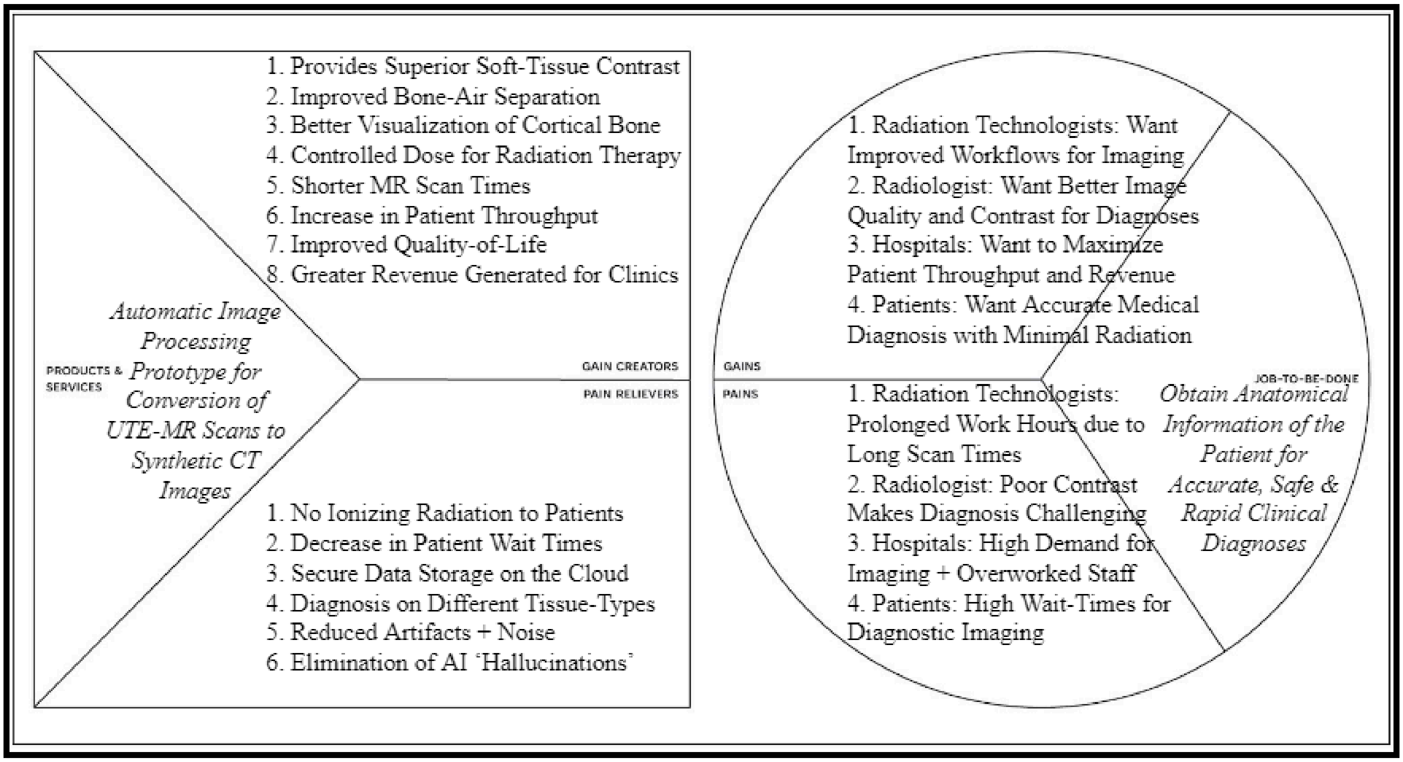


Figure 1. *Customer-Product-Fit Diagram.*

2. Specifications

This section summarizes the critical needs identified for the prototype which were later transformed into requirements. Satisfaction curves with justifications for each metric and a weighted value equation have also been included to facilitate the eventual evaluation of proposed solutions.

2.1. Needs Statements

The following subsection outlines the key components or characteristics of the design which were formulated independent of the possible solutions to the problem. These needs were identified through extensive primary research involving consultations with the client (Dr.

Lumeng Cui from Siemens Healthineers), medical physicists (Asieh Tavakol and Niranjan Venugopal from Cancer Care Manitoba), and research scientists (Dr. Gerald Moran and Dr. Stefan Sommer from Siemens Healthineers). In particular, our meetings with the client were integral for clarifying the scope of the project, setting mutual expectations, and streamlining the research process. Additionally, a thorough literature review was conducted to substantiate the findings from our meetings with the client and other key opinion leaders in the field.

Thus, a set of ten needs were determined which can be classified as either expressed, threshold or latent needs. Expressed needs correspond to fundamental aspects of the design as stated by the primary stakeholder, which is our client. Meanwhile, threshold needs consider unexpressed statements that would cause dissatisfaction for the user if not incorporated. Lastly, latent needs are surplus, unexpected features that would wow the client if included. For the purpose of the formal proposal, we have decided to outline expressed and threshold needs, since their exclusion from the design would render the solution to be ineffective. These are documented as follows (*Table 3*), while latent needs can be found enclosed (*Appendix 1-C*).

Table 3. *Needs Statements for the Image Processing Prototype.*

Key: Expressed Needs (EN), Threshold Needs (TN), Latent Needs (LN)			
ID.	**Description**	**Needs & Values**	**Needs Statement**
1. (EN)	It is incumbent for the image processing prototype to facilitate accurate clinical diagnosis as not doing so would essentially render the design useless. This need goes hand-in-hand with other needs (2, 3, 4, 5) that correspond to enhanced image quality. This can be achieved through implementation of processing techniques that ameliorate parameters such as resolution and contrast while adjusting for noise and artifacts [14]. It is clear that sufficiently and distinctly characterizing the anatomical components within the image would yield improvements in the validity of clinical outcomes.	Accuracy of Clinical Diagnosis	The prototype enhances geometric fidelity via synthetic CT images, thus improving the quality of diagnosis.
2. (EN)	Distinct segmentation of the boundary between cortical bone and air is a prominent issue that current algorithms are still struggling to successfully implement, with many producing 'hallucinations' that	Bone-Air Interface Segmentation	The prototype successfully segments the bone-air interface on UTE MR images, addressing limitations of currently implemented algorithms.

	do not reflect the actual anatomy [15]. Moreover, as stated in literature, achieving correct bone-air segmentation is integral for formulation of electron-density and attenuation-correction maps that guide effective dose exposure for radiation therapy [16]. Hence, it is critical that the design workflow adequately addresses this need through integration of valid post-processing techniques, potentially via use of deep learning methods.		
3. (EN)	Image resolution corresponds to the detail of the information captured, which for medical purposes usually entails the anatomy or physiology of the patient [17]. The client shared that poor resolution is one of the key reasons that led to their most recent synthetic CT AI-product not being widely adopted in the imaging space. Thus, it is essential for the design of the image processing prototype to prioritize achieving good spatial resolution through utilization of noise-reduction techniques.	Image Quality & Resolution	The prototype provides an image with good resolution and minimal artifacts present.
4. (EN)	One of the main issues with the current algorithm implemented for synthetic CT images is poor contrast between bone and soft-tissue. This is particularly problematic as it makes it difficult for radiologists to accurately distinguish between different anatomical structures and to make appropriate diagnoses [18]. Hence, it is critical that the image processing prototype addresses this limitation adequately through UTE-MR imaging.	Bone-Soft Tissue Interface	The prototype successfully preserves contrast for an accurate bone and soft-tissue interface representation.
5. (EN)	As mentioned earlier, the client explicitly stated their desire for the prototype to	Intensity Values	The prototype correctly transforms the intensity values of MRI scans to

	manipulate intensity values via conversion from MRI to CT images. Fundamentally, this would be accomplished by two techniques: inverse logarithmic scaling, which enhances image quality by amplifying darker pixels while compressing brighter pixels, and bias-field correction, which normalizes the image by removing unwanted features not conforming to anatomy, called artifacts [19].	Adjustment	those of CT images by using techniques such as inverse logarithmic scaling and bias-field correction.
6. (TN)	As hinted at during our interactions with the client, adhering to regulatory standards while protecting patient privacy is a non-negotiable feature of the design. Although the data provided would be anonymized with no identifying information of the patients themselves, it is evident that this need must be respected at all times. It is imperative that patient data be guarded and secured, with no unintended leaks occurring within the proposed pipeline [20]. This would be accompanied by thorough research on existing licensing agreements for public, open-source data to ensure that adequate checks are in place before the information is channeled for training of our machine learning component.	Regulatory Compliance	The prototype trains on private and public data as permissible by their license agreement while storing the provided images on a secure, PHIPA-compliant service.

2.2. Requirements

The following subsection focuses on quantifying the technical specifications of our solution based on relevant needs identified previously. These requirements define specific metrics which would serve as parameters to evaluate the performance of our design based on a minimum threshold value. Only those solutions that clear this cutoff value satisfactorily would advance to the next stage of prototyping and development. Supporting literature and justifications have been included to clarify the reasoning behind certain values being chosen to assess proposed solutions. A complete list of our requirements can be found enclosed (*Appendix 1-D*) while a summarized list of our requirements is listed below (*Table 4*).

Table 4. *List of Key Requirements.*

#	Requirement (Need ID)	Value and Type	Justification
1	Spatial Similarity (ID #1)	Must achieve an average symmetric surface distance (ASSD) of less than 1mm.	The geometric fidelity of the generated synthetic CT images from MRI can be evaluated using the ASSD metric, which involves comparing the geometric distances between features in the pseudo-CT and real CT scans [21]. The threshold for the ASSD level MR radiation therapy was researched to be less than 1 mm which is used as the minimum acceptable value [22].
3	Pseudo CT Resolution (ID #3)	Must achieve a spatial resolution of at least 1 mm [23].	The upper threshold for the spatial resolution in a study for CT was identified to be 1 mm [23]. This metric was used to select a minimum threshold of 1 mm for the spatial resolution of our pseudo-CT prototype, as it would be similar to the value obtained from an actual CT image [23].
5	Image Quality + Resolution (ID #3)	Must achieve a Peak Signal to Noise Ratio (PSNR) of at least 20 dB.	PSNR is a widely used metric for measuring the fidelity between the original CT image and reconstructed pseudo-CT image. Based on 22+ studies on synthetic CT generation from MRI using deep learning methods, the median PSNR across studies involving different body parts was between 25-30 dB [5]. However, the deep learning methods used may be too advanced for the scope of our initial prototype. Since 20 dB was the lowest average value across all 22 studies, it would be an appropriate requirement for our image processing pipeline

6	Image Quality + Resolution (ID #3)	Must achieve a Structure Similarity Index Measurement (SSIM) value of at least 0.6.	SSIM is a quality metric that quantifies the loss of structural, anatomical information based on our human visual system by adjusting for parameters such as sharpness, contrast, and brightness [24]. Based on 22+ research papers on synthetic CT generation from MRI using deep learning methods, the lowest SSIM value measured was 0.63 for a study on the brain [24]. Accounting for the conventional workflow of our initial prototype with limited inclusion of deep learning techniques, a minimum SSIM value requirement of 0.6 would be considered appropriate.

2.3. Evaluation Criteria & Value Equation

In this section of our proposal, we will highlight our evaluation criteria, a set of metrics that capture important characteristics of the ideal solution. In our value equation, each evaluation criterion is assigned a weight which reflects the level of importance of the metric within the final solution. Further, each evaluation criterion is represented as a continuous curve with different thresholds corresponding to differing customer satisfaction points given as a percentage: where 100% signifies that the client is fully satisfied while 0% indicates that the client is completely unsatisfied with the solution. Listed in the table below, are further descriptions of key evaluation criteria (*Table 5*). A full list of the criteria can be accessed as follows (*Appendix 1-E, Table A1*).

Table 5. *List of Key Evaluation Criteria.*

1. Geometric Fidelity	
Description: Maintaining geometric fidelity is important for patient safety and accuracy of diagnosis.	**Motivation:** This evaluation criterion is motivated by the need for accuracy of clinical diagnosis. *(See Section 1.5.1, Need 1)*

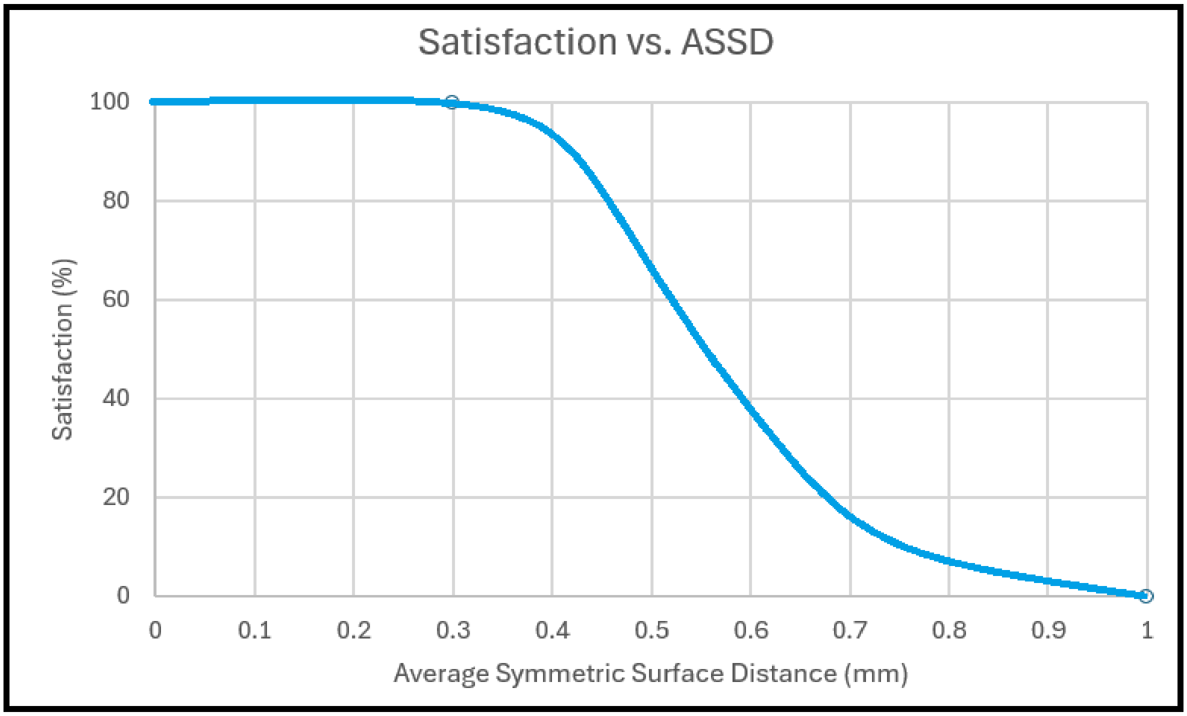


Figure 2. *Satisfaction Curve for Geometric Fidelity.*

Rationale:

A common method for measuring geometric fidelity is the average symmetric surface distance (ASSD) metric. The tolerance for geometric distortion that is generally accepted for MR-only radiation therapy, corresponds to less than 1 mm [22][25]. Any value greater than 1 mm could result in the projection of inaccurate anatomical information, which could seriously hamper the quality of clinical diagnosis. Therefore, an ASSD of 1 mm or above would result in zero satisfaction and thus, would not meet the specified requirements. As observed in the curve, a decrease in the ASSD parameter results in an increase in customer satisfaction. The current application used by the client to generate pseudo-CT images was found to have an ASSD of 0.9 mm and 0.8 mm, for the pelvic region and brain respectively [26]. Ideally, there would be a geometric distortion of 0 mm. However, this is not practically reasonable. As ASSD is measured by comparing a pseudo-CT to a real CT scan there can be differences in the images due to patient movement as well as introduced errors in post-processing, both of which constrain this criteria. Within literature, the lowest geometric fidelity for MRI scanners was found to be 0.3 mm [22]. Thus, 100% satisfaction will be reached at an ASSD value of 0.3 mm or lower.

Tradeoff:

In increasing the spatial resolution the SNR will decrease [27][28]. Lower spatial resolution can increase image distortions, thus decreasing the geometric fidelity [27].

2. Peak Signal to Noise Ratio (PSNR)	
Description: The peak signal-to-noise ratio will be used to measure the quality of the reconstructed pCT image compared to a reference CT image. It is measured in decibels and defined by the equation below [29]. $$PSNR = 20\log_{10}\left(\frac{MAX_f}{\sqrt{MSE}}\right)$$	**Motivation:** The PSNR of the pCT image will be impacted by the pixel intensity differences and would thereby affect subsequent applications and calculations. This evaluation criteria is motivated by the need for accurate clinical diagnosis, bone-air visualization, image quality, and adjustment of intensity values. *(See Section 1.5.1, Needs 1, 2, 3, & 5)*

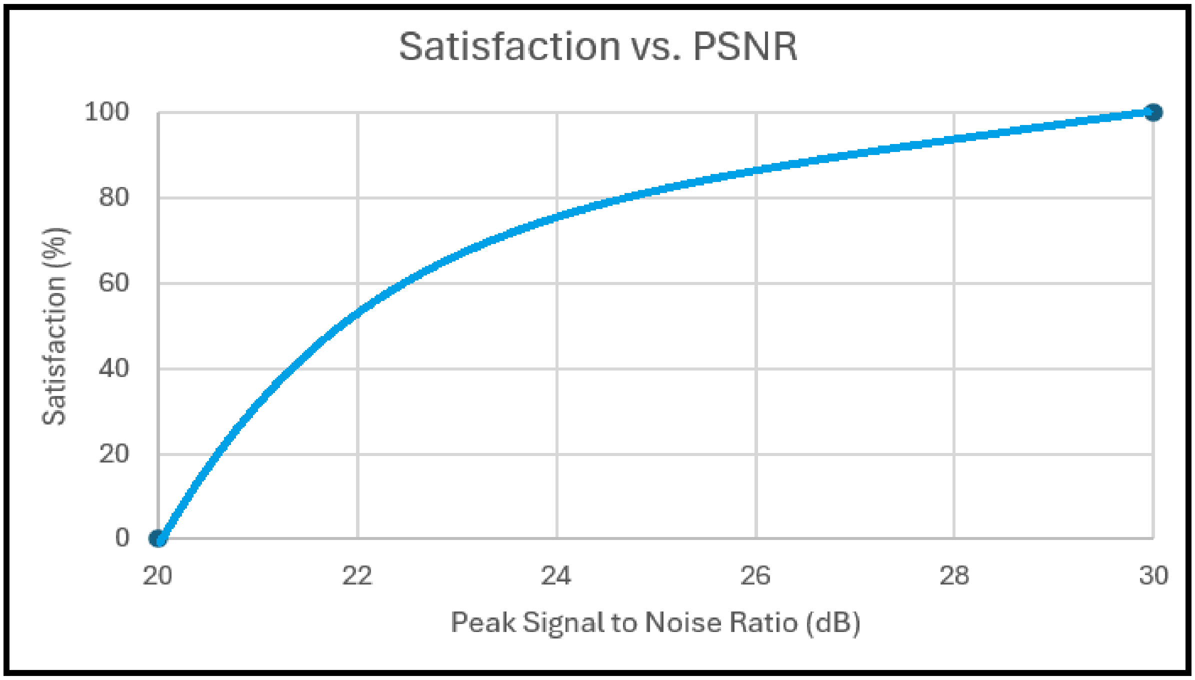


Figure 3. *Satisfaction Curve for Peak Signal-to-Noise Ratio.*

Rationale: Higher PSNR values correspond to better image quality and less noise or distortion in the reconstructed pCT image. Typically, a PSNR of 30 dB or higher is desirable [30]. However, a review of relevant literature revealed that in T1, T2, and zero-time MRI-to-pCT conversions, PSNR ranged in the mid-20s [5]. Therefore, we selected a logarithmic evaluation curve with 0% satisfaction starting at a threshold of 20 dB so as to align with our requirements *(See Section 1.5.2, Requirement 5)*. As a PSNR of 30 dB is considered good quality, the value will result in a satisfaction of 100%. This upholds the tenet that satisfaction increases with PSNR, while acknowledging that it would be unreasonable to expect substantial improvement compared to current state-of-the-art methods.

Tradeoff: PSNR focuses on pixel-wise differences. As a result, this evaluation criterion may not be indicative of the subjective image quality observed by a human radiologist.

3. Image Spatial Resolution

Description	Motivation
Description: The resolution of the resulting image is important in capturing details, thus allowing for more accurate diagnoses.	**Motivation:** One of the listed needs for the product is that the prototype provides an image with good resolution. *(See Section 1.5.1, Need 3)*

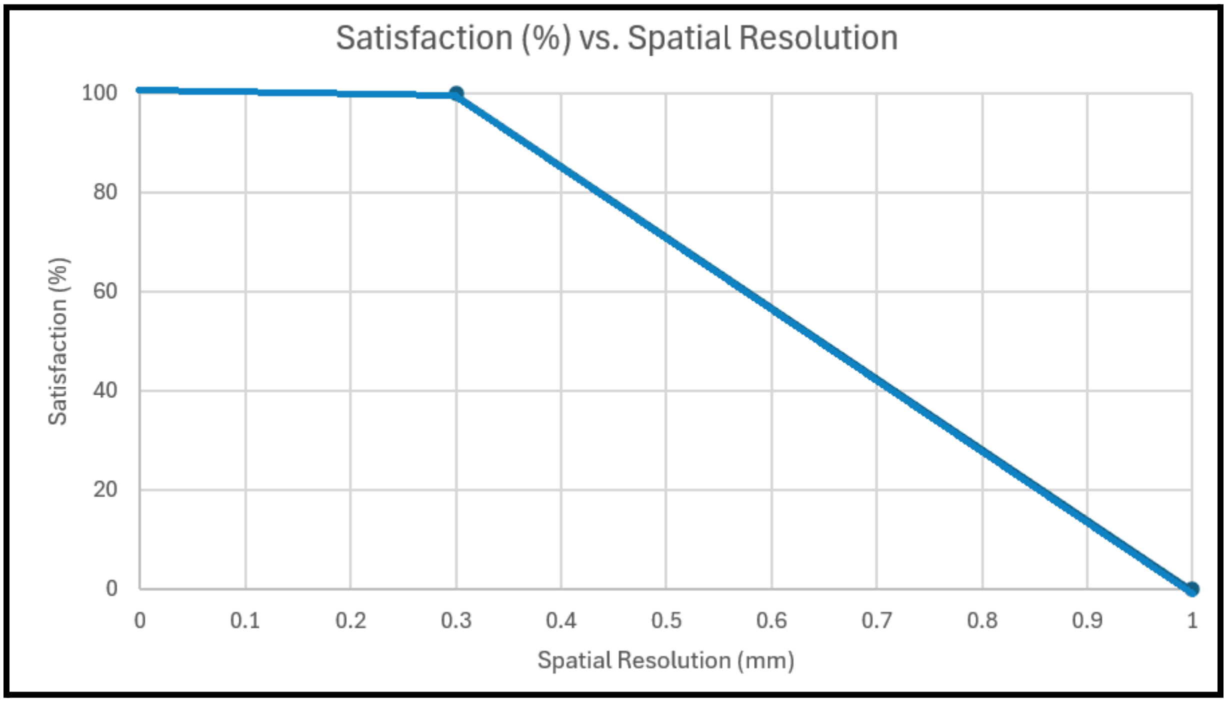


Figure 4. *Satisfaction Curve for Spatial Resolution.*

Rationale:
When discussing the shortfalls of the current AI-based segmentation application with the client, the product's resolution was brought up as one of its key limitations (see Client Meeting #2). The evaluation curve for spatial resolution is linear, a rise in resolution will proportionally increase customer satisfaction. Current single-source CT imaging machines from Siemens Healthcare can obtain a spatial resolution of 0.3 mm [31][32]. Obtaining 0.3 mm spatial resolution would achieve 100% satisfaction. If the generated pseudo-CT images were able to attain a resolution equal to or better than a standard CT image this would outmatch the resolution of current models. In a study that imaged lungs with UTE MRI to generate pseudo CT, a millimetric spatial resolution was obtained [23]. The particular study used the Magnetom Skyra and Magnetom Aera machines from Siemens Healthcare to obtain the MR images.

Tradeoff: Increasing spatial resolution could possibly result in a decrease of temporal resolution, which is a compromise for the prototype.

<table>
<tr><th colspan="2">4. Structure Similarity Index Measurement (SSIM)</th></tr>
<tr><td>Description: The structural similarity index measurement is a quantitative evaluation metric designed to mimic the human visual system, focusing on luminance, contrast, and texture. It is defined by the following equation [24].

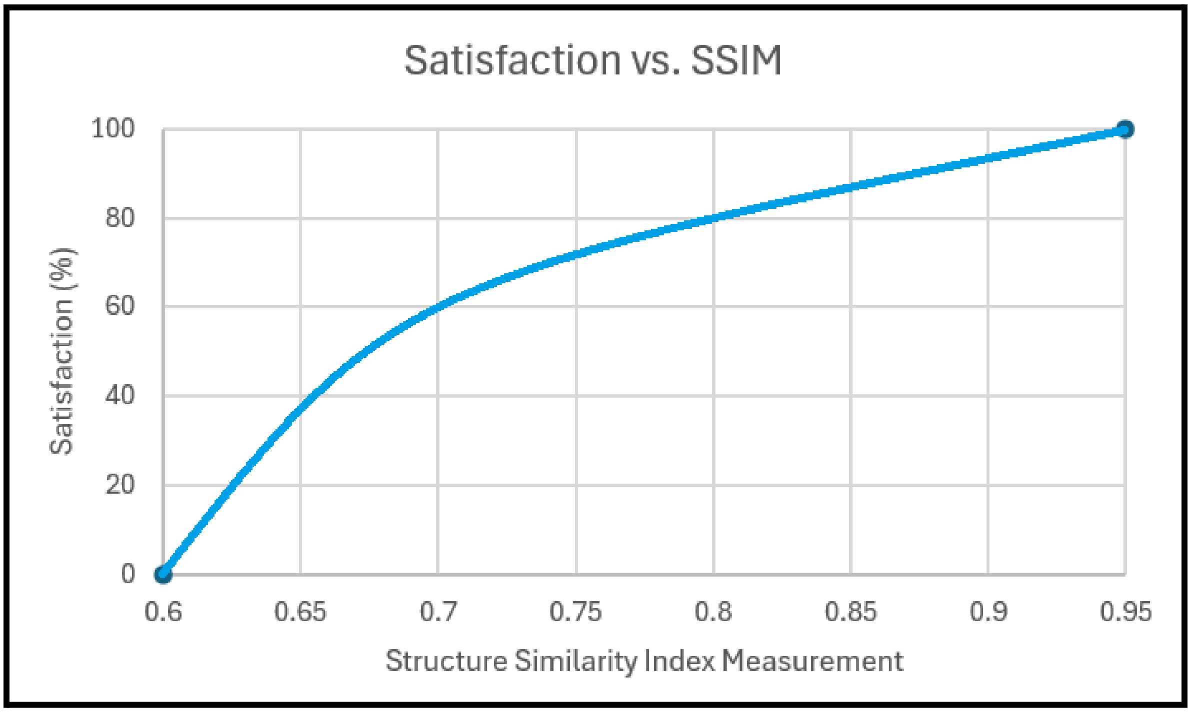
$$S(x,y) = S_1(x,y)\,S_2(x,y) = \left[\frac{2\bar{x}\bar{y}+\epsilon_1}{\bar{x}^2+\bar{y}^2+\epsilon_1}\right]\left[\frac{2s_{xy}+\epsilon_2}{s_x^2+s_y^2+\epsilon_2}\right]$$</td><td>Motivation: The listed needs for our solution include accuracy of clinical diagnosis, performance on different tissues, bone-air interface segmentation, and image quality (See Section 1.5.1, Needs 1,2,3 & 9). The SSIM of the generated pCT image compared to a reference is a good indicator of conversion performance, including interface segmentation and accurate structural representation, which are both important for clinical diagnosis.</td></tr>
<tr><td colspan="2">

Figure 5. Satisfaction Curve for Structural Similarity Index (ASSD).</td></tr>
<tr><td colspan="2">Rationale: SSIM values fall between -1.0 and 1.0, with higher values corresponding to higher similarity in brightness, contrast, and texture in the generated pCT image and reference CT image. The range of 0.9 to 1.0 is typically considered ideal for medical applications, however, one literature review looking at the conversion of MRI to pCT yielded an average SSIM of 0.75 to 0.9 with a global minimum of 0.63 [5]. Thus, we set 0% satisfaction at an x-threshold of 0.60, to align with our requirements (See Section 1.5.2, Requirement 6). A satisfaction of 100% was set at an x-threshold of 0.95 SSIM, as the ideal range for medical application ranges from 0.9 to 1.0 [5]. A logistical curve was selected to represent this relationship to encapsulate the satisfaction region between 0.70 to 0.95 SSIM.</td></tr>
</table>

Tradeoff: Optimizing for higher SSIM may result in prohibitively high computational resources or multi-stage processing pipelines being needed.

Table 6. *Weighted Decision Matrix Based on Evaluation Criteria.*

No.	Evaluation Criterion	Weight	Justification
1.	**Geometric Fidelity**	0.25	Maintaining geometric fidelity is essential for the functionality of the prototype. If used in the clinical setting for radiation therapy it is necessary that the patient's anatomy is correctly represented. Otherwise, this could lead to increased unnecessary ionizing radiation to healthy tissues. Thus, this criterion has one of the highest weightings.
2.	**Peak Signal-to-Noise Ratio**	0.25	The peak-to-signal noise ratio will impact the images' pixel intensity differences. This is especially important in differentiating bony structures in MR images. Knowing that one of the challenges in creating pseudo-CT from MRI is the low contrast of bone, we ranked this criterion as another one of the highest weightings.
3.	**Image Spatial Resolution**	0.20	Geometric fidelity, peak signal-to-noise ratio, and structure similarity index are all interdependent on one another resulting in similar weightings for each of these criteria. Obtaining high spatial resolution would allow for the capturing of finer details which can be of importance in defining tissue boundaries. While it is still important to the solution and ranked highly, we believe it is slightly less important than geometric fidelity and peak signal-to-noise ratio due to the goal of this project.
4.	**Structure Similarity Index Measurement**	0.20	The structure similarity index provides an overall quantitative analysis. While this criterion is important in quantitative evaluation, the other two metrics provide more detail and specifics rather than a general assessment.
5.	**CT Number Accuracy**	0.10	This criterion was given the lowest weight as it was specified by the client that evaluating CT numbers would be an additional plus to the prototype and not required.
SUM		1	

<u>Value Equation:</u>

$$Value = 0.25\times EC_1 + 0.25 \times EC_2 + 0.2 \times EC_3 + 0.2 \times EC_4 + 0.10 \times EC_5$$

Note: EC_x corresponds to evaluation criterion 'x'.

3. Work Plan

The following section includes details for the project roadmap, team roles and expectations as well as the required resources and budget for the design process.

3.1. Project Roadmap

The Gantt chart provided below summarizes the major deadlines and work plan for major stages for our project: Ideation, Detailed Development and Validation (*see Figure #6*). Budgeting is also included as a key component to ensure that financial and miscellaneous resources used in the course are accounted for in a timely fashion. This chart acts as a roadmap to streamline the design process and to ensure that tasks are completed successfully within the project timespan.

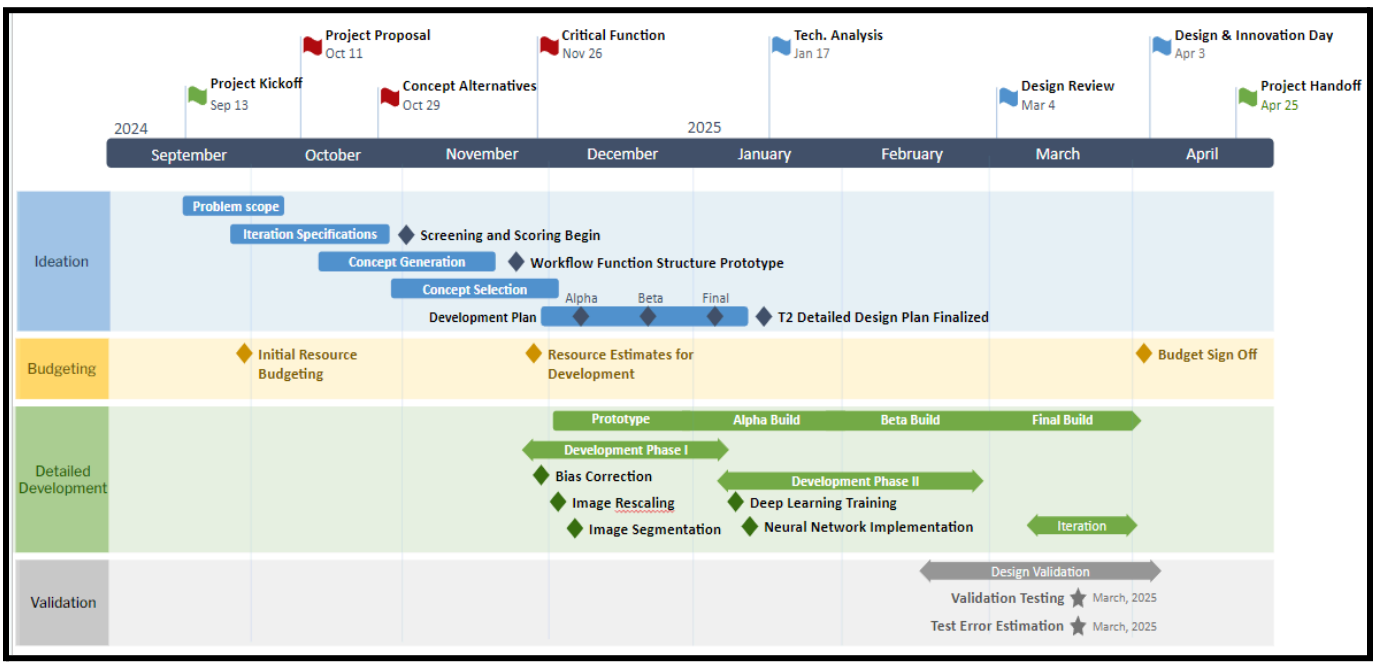


Figure 6. *Project Gantt Chart Across 8-Month Timeline.*

3.2. Team Roles & Expectations

Team roles have been assigned to each member based on their interpersonal skills, technical strengths and holistic ability to positively contribute to the project (*see Table 7, 8*).

Table 7. *Roles and Responsibilities Assigned to Each Member of the Team.*

Project Role	Assigned Member(s)	Description
Project Coordinator	Aly Khan Nuruddin	This individual is responsible for coordinating the project workflow, which includes maintaining timelines, delegating tasks and scheduling team meetings.
Client Liaison	Aly Khan Nuruddin	This member is responsible for communicating with the client, course instructors and faculty supervisor via email and MS Teams. Additionally, the liaison would schedule meetings and inform the team about communications from the client and faculty supervisor in a timely manner.
Editor	Manan Verma, Lynn Alvarez Krautzig	These members are responsible for making the final edits on all documents that are to be submitted and complete the submission process. Both individuals will take turns proofreading documents and will edit the final draft together.
Notetaker	Manan Verma, Lynn Alvarez Krautzig	These members are responsible for taking minutes for client and faculty supervisor meetings.
Technical Manager	Yuheng Zhang, Jackson Chen	These members are responsible for sourcing relevant equipment and resources needed for the project.

Financial Manager	Yuheng Zhang, Jackson Chen	These members are responsible for managing the team's overall budget and for handling reimbursements.

Table 8. *Specialization & Strengths of Each Member of the Team.*

Team Member	Specialization	Strengths
Aly Khan Nuruddin	Systems & Signals	Image Processing, Programming, Machine Learning, Data Analysis
Lynn Alvarez Krautzig	Systems & Signals	Medical Imaging, Programming
Manan Verma	Bioinformatics	Programming, Medical Imaging, Machine Learning, Data Analysis
Jackson Chen	Bioinformatics	Programming, Algorithm Design, Software Engineering
Yuheng Zhang	Bioinformatics	Programming, Scripting, Software Engineering

3.3. Required Resources & Budget

The resources and budget allocated for completion of both workflows is succinctly summarized below with justifications for the cost provided as well (*see Table 9*).

Table 9. *Required Resources and Budget for the Project.*

Item	Quantity	Cost Per Unit	Total Cost	Notes
TASK 1: CONVENTIONAL WORKFLOW				
Personal Computer	1 Per Student	$0	$0	Each student can use their personal computer to carry out the technical, image processing techniques required for the task.
Python: Programming Language [34]	1 Per Student	$0	$0	A free open source programming language used for the entire processing workflow across both tasks.

				Many libraries currently exist for medical imaging, which can be implemented to make the image processing pipeline more efficient [35].
3D Slicer: Medical Imaging Software [36]	1 Per Student	$0	$0	A free open source application for medical image viewing and analysis.
Jupyter Notebook: Interactive Web Application [37]	1 Per Student	$0	$0	An online platform to create interactive notebook documents with code and equations that can be run live. This is useful for displaying the workflow steps in a presentable format.
GitHub: Collaborative Code Repository [38]	1 Per Student	$0	$0	A developer platform used for code collaboration and version control. This will be used to manage the codebase.
Google One: Cloud Storage Platform [39]	1	$3.99 / month (200 GB)	$23.94 for 200 GB (6 months)	A cloud storage plan for storing and accessing all the medical images in the dataset. 200 GB was estimated to be sufficient based on the estimated dataset size. Additionally, the platform can be used down the road for storing deep learning models and outputs.
TASK 2: ADVANCED WORKFLOW WITH AI				
Google Cloud: Compute Instance with Graphical	1	$60-80/month	$240-320 (4 months)	A virtual machine (PC emulator) that runs on Google infrastructure, which allows for better

Processing Unit (GPU) [40]				scalability and portability. This way, the computationally intensive tasks can be run in a self-contained environment, minimizing the footprint of personal computers. Moreover, the software is validated for the FIPS 140-2 encryption module and is compliant with the Canadian Personal Health Information Protection Act (PHIPA). Hence, the virtual interface is secure for storage of confidential data and for safeguarding patient privacy. Prices are dependent on many factors, such as number of CPU cores, hours of use, memory amount and GPU selection, etc. The price range selected is for a specific configuration with each instance running 8 hours a day [41], which should be sufficient for our task. We have chosen a 4 month duration as the development process will span from December, 2024 to March, 2025.
TensorFlow [42] or PyTorch [43]: Machine	1 Per Student	$0	$0	These free open source Python libraries will be used for deep learning model development. Whether we choose

Learning Libraries				TensorFlow or PyTorch will be decided later, as this selection depends on our prior, conventional workflow implementation.

The first task corresponds to conventional image processing for which free applications and web-based resources should suffice. This work can be achieved on personal computers as the overall computing power required is not extreme. However, as mentioned by the client, we are encouraged to seek existing open-source solutions which may require additional computational resources and could potentially incur extra costs (*Appendix 1-G*). Further, accessing certain studies for literature research beyond the UBC Library platform may require a paid access plan. For the second task, we will need advanced computing resources since training and running a deep learning model is heavily dependent on the speed of the computer. Given the timeliness required to adequately build, fine-tune and validate the machine learning networks, it is probable that the team may purchase more computing power. The GPU instance selection will depend on our specific implementation, so the exact cost would not be finalized until the second term.

BMEG 457 – Design History File (DHF) 2.

December 06, 2024

Client: Siemens Healthcare Ltd. (Siemens Healthineers Canada)

Project: Magnetic Resonance Imaging (MRI)-Based Pseudo Computed Tomography (pCT) Generation Using Ultrashort Echo Time (UTE) Technique

Team #17: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen

Faculty Supervisor: Tim Salcudean

THE UNIVERSITY OF BRITISH COLUMBIA

Report Type: Iterating Specifications

Section Word Count: 2803

Abstract

The following document summarizes additional constraints involved in implementation of Magnetic Resonance (MR) for radiation treatment planning. Moreover, the report creates benchmarks for existing solutions, defines regulatory considerations, and modifies specifications.

VI. *Table of Contents*

VII. *List of Tables & Figures*

4. Benchmarking Existing Solutions

The most promising alternative solutions as identified previously (*Section 1.3*), along with other favorable concepts from additional research, were used for benchmarking against key specifications (*Section 2*). To enable ease of comparison between current state-of-the-art solutions, quantifiable metrics were obtained from existing literature for the outlined requirements. These comparisons would help us in identifying relevant areas of improvement for our minimal viable prototype. Moreover, these benchmarks would facilitate evaluation of our solutions's performance when compared to current digital products in the market (*Table #10*). However, the values for two benchmark metrics, ASSD and SSIM, were unable to be determined from our literature review of synthetic CT generation for the Random Forest model.

To be noted, 'Pseudo CT Resolution', which was a requirement identified in the previous report, was removed from consideration following client consultation. Dr. Lumeng specifically clarified that spatial resolution is preset based on scanner settings, and therefore is already taken care of in acquisition of the input MR image. In other words, this parameter cannot be modulated through the post-processing routine, and is thus, not applicable as a valid requirement to assess the performance of our concepts. As our workflow is designed to generate pCT from provided MR images, spatial resolution would no longer be a defining specification for future analysis.

Table 10. *Benchmark Comparisons for Existing Solutions.*

Specification	Benchmark	sCT using Random Forest	sCT using Multi Cycle GAN	sCT using DCNNs
Spatial Similarity - Geometric Accuracy between Pseudo CT and True CT	Average Symmetric Surface Distance (ASSD) in mm		4.21mm [44]	4.59mm on CT 7.58mm on MRI classification [45]
Accurate Intensity Distribution - Synthetic CT Image Accuracy	Hounsfield Units (HU)	57.45 HU [46]	0.0416 HU [47]	71.1 HU on average for T2 [48]
Image Quality + Resolution -	Structure Similarity Index Measurement		0.97 [49] - Estimated the	0.95 [48]

Structural Similarity Based on Comparison with CT Images	(SSIM)		value from a cycleGAN for sCT generation	
Image Quality + Resolution - Accurate overlap of Anatomical Structures between Pseudo and Actual CT	DICE Similarity Coefficient	0.84 for bone 0.98 for air [50]	0.8085 [44]	0.83 for bone threshold 0.99 for body [51]
Image Quality + Resolution - Quality of the Constructed pCT Image	Peak Signal to Noise Ratio (PSNR) in dB	28.33 dB [47]	39.1 dB [47]	29.44 dB [47]

5. Regulations, Classifications & Best Practices

5.1. Regulatory & Classification Considerations

As mentioned previously in our needs statements (*Section 2.1*), complying with existing regulatory standards (Need #6) is a fundamental 'threshold' need for the design. Not acting in accordance with this tenet would cause significant dissatisfaction for our primary stakeholder, the client. Given the potential clinical applications of our imaging prototype for radiology scanning, disease diagnoses and prognostic guidance, there are certain regulatory concerns that arise pertaining to image conversion accuracy, data security, and patient privacy.

Our primary expressed need from client consultation pertains to the accuracy of depicted anatomical structures following conversion from MR to pseudo-CT scans (Need #1). It is crucial that the output images are of sufficient quality, and satisfy evaluation criteria for region-based (DICE Similarity) and voxel-wise (Mean Absolute Error, Spatial Similarity, Structure Similarity, Peak Signal-to-Noise Ratio) metrics. Hence, the prototype would require extensive validation against gold-standard CT images to corroborate its effectiveness for medical use.

The other significant consideration involves safeguarding the provided clinical images and obtaining appropriate permissions for use of open-source data. A secure, online platform that is compliant with the privacy policy outlined for our jurisdiction of operation, which is Canada, would need to be utilized to store the given datasets. Microsoft Teams, for example, is a widely available proprietary file storage system that adheres to over 90 regulatory laws globally, and would thus, be a suitable candidate for integration with our processing prototype [52]. Moreover, to avoid embroilment in legal battles, adequate licensing agreements would need to be acquired before consolidation of public datasets for training of the machine learning models. Adherence to the signed AI Tool Approval Form would also need to be upheld consistently during the project. Correspondingly, the use of Generative AI platforms would be kept at a minimum and only for menial tasks to avoid compromising confidential, company-specific information to the public.

The following table summarizes current health and industry licensing protocols for three primary jurisdictions: United States, Canada and European Union. These markets would serve as promising target markets with appropriate financial and technological infrastructure in place to support the digital installation and distribution of our prototype (*Table 11*). Major governmental bodies involved in regulating the implementation of our solution are also mentioned below.

Table 11. *Regulatory Considerations for our Prototype.*

Jurisdiction	Classification	Health and Industry Licensing Qualifications & Considerations
United States	Food & Drug Administration (FDA) Class II (or III)	Our project qualifies within the Software as a Medical Device (SaMD) category under FDA guidelines [53, 54]. From the FDA classification for radiology devices, the Computed Tomography (CT) X-ray system includes signal analysis, display equipment, patient and equipment supports, component parts and accessories [53]. As the image processing prototype for generating pCT images would likely act as a substitute for true CT under certain clinical scenarios, it can be considered a Class II device due to its impact on diagnostic outcomes. This classification may be elevated to Class III in cases where generated images are used to determine radiation dosages. Examples of quality assurance regulations that may be imposed as a result of Class II/III designation include the requirement of a 510(k) premarket notification, [55] and standardized verification according to guidelines outlined by ISO 13485 [56].
Canada	Health Canada Class II (or III)	Similar to FDA classification, Health Canada guidelines would also categorize our MRI to pCT image processing prototype as SaMD [57]. Therefore, with its role as a facilitator of clinical diagnosis, the device would be assigned a Class II designation under the Canadian legislation's definition of an active diagnostic product [58]. The device may be promoted to Class III in cases

		where output of the segmentation model would be used to aid in calculation of doses for radiation therapy [59]. Devices classified into Class II or above are required to obtain a Medical Device License (MDL) [60] before distribution in Canada. To acquire this licensing, compliance of appropriate Quality Management Services (QMS) towards established validation and verification frameworks must be performed and well documented. In addition to ISO 13485 [56] standards for medical devices, MDL also recommends implementing ISO 14971's tenet of software risk management [61]. Throughout the development of our project, we would also need to conform to the Canadian Personal Information Protection and Electronic Documents Act [62]. As mentioned, this signifies that data must remain decoupled from the provider, as medical records and any other identifying content are considered as confidential information under the Personal Information Protection and Electronic Documents Act (PIPEDA) [63].
European Union (EU)	Conformité Européenne (CE) Certification for Medical Device Regulation (MDR) - Class IIa (or IIb)	Our MRI to pCT image processing prototype would be categorized as a SaMD in Europe, which is classed as an active device by the EU 2017/745 regulation [64]. As the product would be licensed for use in clinical settings, it would need to undergo Medical Device Regulation (MDR) [65] in order to obtain a European CE Marking. This is a necessary step prior to distribution and usage in the European Economic Area [66]. For the purposes of MDR, Class IIa designation would be applied as the project is "intended to provide information used to make decisions with diagnosis or therapeutic purposes" [67]. If the image processing prototype would be used to inform decisions that could cause serious deterioration in health or surgical intervention, this classification could be upgraded to IIb [67]. Next, implementation of a QMS would occur in accordance with the MDR. Similar to the FDA and Health Canada, this QMS includes clinical evaluation, post-market surveillance and a Post-Market Clinical Follow-Up (PMCF) plan [68]. This would apply standards for software risk management from ISO 13485 [56] and potentially ISO 14971 [61] to our medical device.

5.2. Best Practices

Established market standards for medical image processing are generally codified within regulatory frameworks and vary widely based on different professional societies in the field. To simplify the process of curating such guidelines, the following section would solely focus on discipline-specific associations in North America (Canada, United States), such as the Canadian Organization of Medical Physicists and American Society of Radiologic Technologists [69]. However, if needed, best practices from other professional bodies in the European Union, Asia and Australia could also be included to increase robustness of the design process. This would be determined through subsequent communications with the client following further prototyping.

While the above-mentioned organizations provide a thorough outline of the safety precautions for radiologic purposes as well as appropriate data acquisition practices, those are beyond the scope of this project. Instead, to develop our prototype, it is important to consider optimizing various components of the computational workflow which include training, testing, validation and deployment of the model. While implementing the deep learning-based synthesis, images must be binned into different train, test, and evaluation datasets to ensure reliability of outcomes. Additionally, sufficient data must be available with ample diversity to avoid biasing the results. It is also critical to comprehend that each machine learning approach would have its own limitations. Hence, any results obtained must not be considered as 'absolute' in terms of its performance. Instead, sufficient error analysis must be conducted to quantify the variance and misclassification rate of the model. Lastly, the workflow must consider both statistical and clinical validation procedures such as crossfolds and histogram analysis respectively, to verify independent results against ground-truth CT images [70]. Adhering to the above guidelines would help inform better training and testing practices, increasing the robustness of our solution.

6. Updated Specifications

The following section outlines improvements to our specifications from the previous report (*Section 2*), with revisions to needs (*Section 2.1*), requirements (*Section 2.2*), and evaluation criteria (*Section 2.3*). Through conversations with the client, our specifications were updated to better reflect the expectations of our stakeholders at Siemens Healthineers. The meeting minutes from our conversations with Dr. Lumeng Cui, Gerald Moran and Stefan Sommer provide relevant documentation, and can be found enclosed (*Appendix 1-H, 2-A, 2-B*).

6.1. Revised Needs Statements

Based on our needs statements (*Section 2.1*), two additions were made to encompass the regulatory considerations for our device, as indicated below (*Table 12*).

Table 12. *Revised Needs Statements with Justification for Inclusion.*

Specification	Revised Specification	Justification
NEW	The prototype meets Health Canada's regulation for Class II SaMD	Under Health Canada's guidelines, our product would be classified as Software as a Medical Device (SaMD). In particular, it would be categorized as a Class II software, since it is an active diagnostic tool for use under clinical supervision [71, 72]. The device would therefore require a Medical Device License (MDL) prior to distribution in open markets to ensure compliance with the Class II designation [73].
NEW	The prototype complies with the Canadian Personal Information Protection and Electronic Documents Act (PIPEDA).	The Canadian Personal Information Protection and Electronic Documents Act mandates all datasets utilized by software products for analytical purposes to be anonymized [74, 75]. Therefore, it is of utmost importance that datasets provided by the client are not distributed to any third parties and do not contain any identifying patient information. Kindly note that this has been documented previously in the AI Approval Form, which was compiled in correspondence with the client.

6.2. Revised Requirements

Based on our revised requirements (*Section 2.1*) and through client consultation, the spatial resolution requirement was removed in favor of the DICE similarity score *(Table 13*).

Table 13. *Revised Requirements with Justification for Removal or Inclusion.*

Specification	Revised Specification	Justification
Pseudo CT Resolution Must achieve a spatial resolution of at least 1 mm	REMOVE	The spatial resolution of the output pCT would be dependent on the input MR image used to generate it. Meanwhile, the resolution of the MR image is determined by the acquisition process, with longer scanning times resulting in better numbers. While certain post-processing techniques

		such as interpolation can improve the 'perceived' resolution, the image generated is fabricated and does not represent authentic anatomical information. Additionally, the workflow designed to generate pCT is not concerned with the acquisition process of the MR images, which would simply be provided to us by the client. Hence, spatial resolution of synthetic CT images would no longer be considered a suitable requirement to quantitatively validate the performance of our image processing prototype.
NEW	*Requirement #5: Image Quality + Resolution* Must achieve a DICE score above 0.83.	In addition to measuring the SSIM of the generated pCT, the client suggested exploring other region-based metrics to evaluate similarities between the pCT and ground truth, 'real' CT image. One of the measurements mentioned by Dr. Lumeng was the DICE similarity coefficient [76], which ranges between 0 (no similarities) to 1 (identical images). In studies investigating the DICE similarity coefficient of pCT images generated from MR data, values between 0.83 to 0.94 were most commonly recorded [77, 78]. Hence, the minimum requirement for this criterion is set to be greater than 0.83 to capture sufficient similarity between output and test scans.
NEW	Must meet ISO 13485 standards.	The design must satisfy ISO 13485 standards to ensure that it satisfactorily achieves regulatory standards under the Class II SaMD categorization [79].

6.3. Revised Evaluation Criteria

The evaluation criteria below reflect the changes made to our requirements in the previous section, with a new satisfaction curve added for the DICE similarity score (*Table 14*).

Table 14. *Revised Evaluation Criteria with Satisfaction Curves.*

Specification	Justification

<table>
<tr><td><u>Image Spatial Resolution</u>

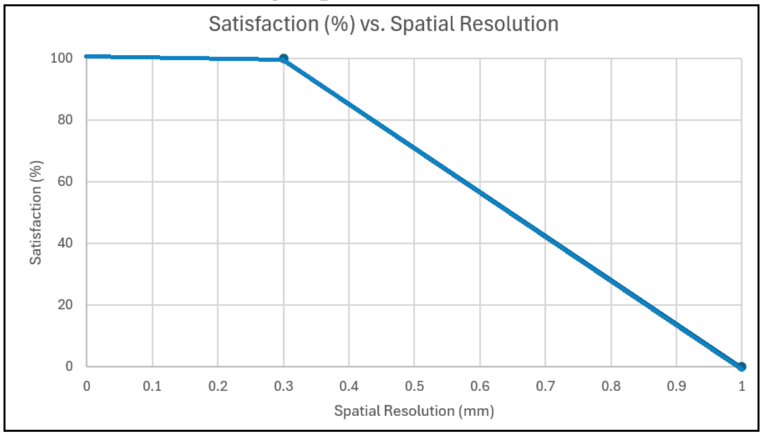



Figure 7. Satisfaction Curve for Spatial Resolution</td><td rowspan="3">From our client meetings, it was made clear that the initial values selected for this evaluation criterion were over optimistic. MR imaging inherently has lower resolution numbers than CT scans. The typical resolution for output images from a CT scanner is 0.3mm. Hence, it would be nearly impossible to replicate the same values for a pCT image generated from input data taken via a lower resolution MR scanner.

The workflow designed to generate pCT is not meant to replace CT entirely, and instead focuses on giving complementary sources of diagnostic information. Achieving an equal spatial resolution to CT is therefore not a necessity for this project.</td></tr>
<tr><td>Revised Specification</td></tr>
<tr><td>We will remove this evaluation criterion from our Weighted Decision Matrix (WDM) and it would therefore play no role in the assessment of our selected solution.</td></tr>
<tr><td>Specification</td><td>Justification</td></tr>
<tr><td>NEW</td><td rowspan="3">As aforementioned (Table 13), current values in literature were found to be between 0.83 to 0.94. The client would be unsatisfied if the solution obtains a DICE score of 0.83 or less. However, user satisfaction increases linearly until 0.94, which would fully fulfill expectations. As the DICE coefficient rises, the accuracy of the human anatomy mapped from the MR to the pCT image also</td></tr>
<tr><td>Revised Specification</td></tr>
<tr><td><u>DICE Similarity Coefficient</u></td></tr>
</table>

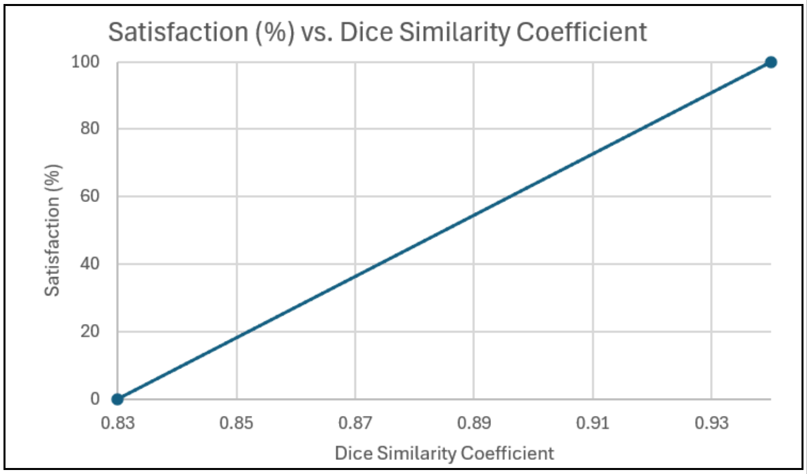


Figure 8. *Satisfaction Curve for DICE Similarity Coefficient*

increases, and so would our confidence in the device's function.

As an evaluation criterion was removed while another was added, further revisions were made to our Weighted Decision Matrix (*Table #15*). Further, after our client meeting, we gained a better understanding of the significance of each criterion for ranking of our potential solutions. Therefore, the weights for the Value Equation were updated to reflect this change (*Table #16*).

Table 15*. Revised Weighted Decision Matrix Based on Updated Specifications.*

Specification	Revised Specification	Justification
Peak-Signal-to-Noise Ratio Original Weight: **0.25**	*Peak-Signal-to-Noise Ratio* Modified Weight: **0.15**	As mentioned in *Section 4*, after consultation with the primary stakeholder, our team was advised that the majority of the PSNR is generated from the acquisition process. While the workflow is not focused on improving the acquisition process, certain processing techniques can be implemented to improve the PSNR. However, this could be challenging to implement using standard pre-processing methods such as bias field correction and inverse log scaling, as well as post-processing approaches such as noise removal. Based on this information, the group decided to lower the weight for this particular criterion by 10%.

NEW	*DICE Similarity Coefficient* Assigned Weight: **0.25**	The DICE similarity coefficient provides an alternative form to quantitatively evaluate the performance of our output data. Hence, this metric would provide us with some reassurance when testing for similarities between the processed pCT and provided true CT images. A weight of 25% would be allocated to this criterion, similar to the value for the structure similarity index measurement.

Table 16. *Summarized Revised Weightings for Each Evaluation Criterion.*

No.	Evaluation Criterion	Weight
1.	Geometric Fidelity	0.25
2.	Peak-Signal-to-Noise Ratio	0.15
3.	~~Image Spatial Resolution~~	REMOVED
4.	Structure Similarity Index Measurement	0.25
5.	CT Number Accuracy	0.10
6.	DICE Similarity Coefficient	0.25
SUM		1.0

BMEG 457 – Design History File (DHF) 3.

December 06, 2024

Client: Siemens Healthcare Ltd. (Siemens Healthineers Canada)

Project: Magnetic Resonance Imaging (MRI)-Based Pseudo Computed Tomography (pCT) Generation Using Ultrashort Echo Time (UTE) Technique

Team #17: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen

Faculty Supervisor: Tim Salcudean

Report Type: Concept Generation

Section Word Count: 4951

Abstract

The following document proposes concepts for an automatic processing prototype. that converts an Ultrashort Echo Time Magnetic Resonance (UTE-MR) image into a pseudo-CT. A function structure diagram was first generated to identify the most significant components of the software workflow. The concept generation phase built upon the critical functions established previously by shortlisting relevant promising approaches from recent literature. Finally, through quantitative assessment via concept screening and scoring, a clear favorite emerged for implementation in future design iterations for our deep learning-based image segmentation module.

VIII. *Table of Contents*

IX. *List of Tables & Figures*

7. Function Structure Diagram (FSD)

Following exploration of our evaluation criteria (*Section 2.3*) and through regular consultations with our client, a Function Structure Diagram (*Figure 9*) was created to accurately capture the primary components of our potential solution. Our workflow begins with capture of the MR images via a configured scanning system that implements an Ultrashort Echo Time (UTE) sequence to highlight bone contrast. Next, our prototype would perform preprocessing on the acquired images to correct contrast levels utilizing bias correction and inverse logarithmic scaling, followed by thresholding of anatomical structures using histogram peaks. This is proceeded by segmentation, where cortical bone is first distinguished from air and then later, from soft tissue. Deep-learning based methods would then be applied to enhance our segmentation performance (*See Section 9*). Lastly, following removal of artifacts, our pseudo-CT results would be validated based on the evaluation criteria (see *Tables 21-23*), and displayed in real-time. Our determinative functions, which are the most crucial operations in the workflow required for achieving accurate results. These include pre-processing, segmentation, and statistical validation, as illustrated in pink within our FSD below. Meanwhile, as shown by the green arrow, energy transfer occurs solely during acquisition while the remaining functions inside and outside the software boundary only consider information transfer, as shown in red.

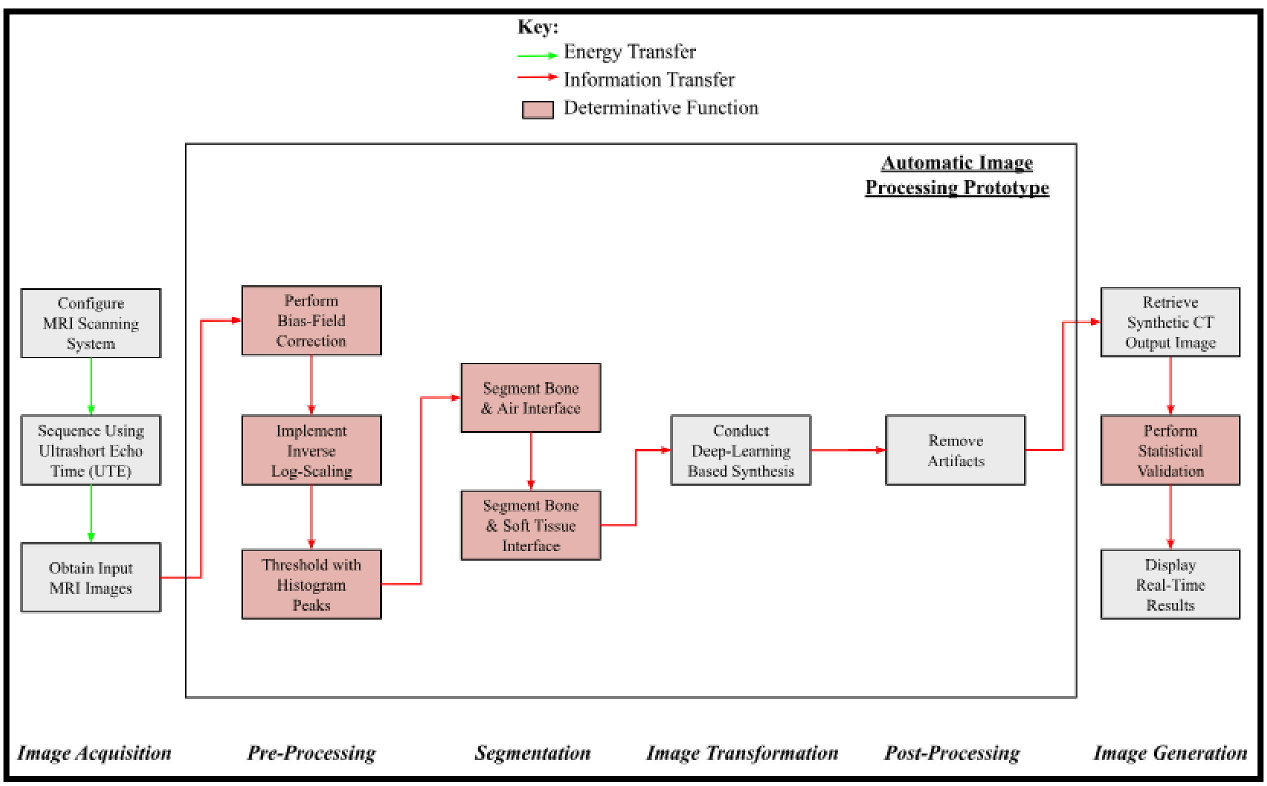


Figure 9. *Function Structure Diagram of the Proposed Workflow.*

8. Concept Generation

After outlining the determinative functions in our FSD, a thorough literature review was performed to identify the most promising concepts. An important point for consideration is that the majority of functions within our solution were pre-determined by the client and laid out in a specific order. Therefore, the deep learning-based synthesis provides us with an appropriate avenue to conduct concept generation and selection for our design. As mentioned by Dr. Lumeng, the machine learning methods outlined below can be considered as an 'add-on' or 'bonus' feature to optimize the workflow of our existing prototype. Our initial concept generation involved identifying 5 general frameworks through research from the extensive list of methods currently available, before refining these ideas further (*see Section 10*) (Table 14).

Table 14. *Evaluation of Most Promising Initial Concepts.*

Concept #1: Generative Adversarial Networks (GAN)		
Feasibility	**Requirements**	**Technical Readiness**
This model is widely utilized in medical imaging for segmentation and classification purposes [80]. Multi-Cycle GANs in particular facilitate unpaired training, which is useful for augmenting images from imbalanced classes [81]. Recently, Stacked GANs are being explored with specific applications for radiation therapy planning and disease diagnoses [82]. By combining the decoding and encoding within the same architecture, the model has shown greater promise for pseudo-CT images compared to existing methods such as NSFs and CycleGANs. Alternatives that incorporate convolutional networks as well as conditional and semantic information, such as AGGANs WGANs and ProgressiveGANs would also be explored [84].	Based on our updated list of specifications highlighted in DHF-2 (*Section 6*), this concept sufficiently meets all the requirements. SSIM values of around 0.92, DICE score of 0.86 and mean PSNR of 0.24 have been observed via use of Multi-Channel-Multi-Path GANs. Additionally, an MAE of 227 HU with mean difference of 85.8 HU was obtained for Single-Channel-Single-Path GANs [84].	There are several readily available libraries for multi-scale implementation of GANs. Within the Python development environment, TF-GAN and STUDIOGAN open-source modules are applicable for use with PyTorch and TensorFlow, respectively [85]. A pre-trained GAN synthesizing network for medical imaging called medigan, can also be conveniently sourced from GitHub [86]. The module is compatible with Python and can be used to create synthetic datasets to train our GAN model.
Concept #2: Random Forests		

This model has made use of probability maps for accurate segmentation of bone, air and soft tissue [87]. Quite interestingly, this method has previously been successfully implemented and even performed better than some GANs [87].	This concept met the key requirements based on our updated specifications for benchmarking *(Section 4*). An intensity distribution of 57.45 HUs, as well as DICE similarity scores of 0.84 for bone and 0.98 for air, were observed [87]. It also achieved a PSNR of 28.33 dB [88] . However, values for ASSD and (SSIM) metrics were not available in literature, thereby its geometric accuracy could not be accurately determined.	Random Forests are widely implemented in machine learning libraries such as Scikit-Learn [89]. These open source models are easily available and have supporting documentation available for guidance.
Concept #3: Deep Convolutional Neural Networks (DCNN)		
This model has a proven ability to learn spatial patterns and map differences in contrast and tissue representations between modalities [90]. Additionally, this method has a very fast time for computation during deployment and can suitably accommodate large amounts of training data [91].	Based on the benchmarked specifications (*Section 4*), this model met the requirements of sCT, with an image accuracy of 71.1 HU and DICE similarity coefficient of 0.83 and 0.99 for bone and body, respectively. Additionally, the concept also fairly exceeded expectations for resolution with a PSNR of 29.44 dB [88, 92,93]. However, a geometric accuracy of 4.59mm on CT and 7.58mm on MRI, with an SSIM of 0.95, signifies that the solution did not meet these requirements [92, 94].	Deep Convolutional Neural Networks are a popular method in the world of machine learning. Plenty of well-known libraries like TensorFlow and PyTorch exist for building DCNNs [85, 95]. However, most models are trained to classify images, so a more specific implementation would be needed to accomplish the specific tasks of the project.
Concept #4: Ensemble Methods		
Ensemble learning methods with multi-regressors and deep learning inputs are infrequently used to pool strong models together, reducing noise and variance. In particular, current methods include Ensemble Deep Learning (EDL), where	The multi-regressor ensemble with INAR resulted in a DICE similarity coefficient of 0.81, falling below our requirement of 0.83 (*See Table 13, Section #6*). This could be construed as a pass with potential revision or developmental	Ensemble methods like bagging, boosting, voting, etc. are commonly known in ML spaces. There are various repositories in OpenCV that provide Jupyter notebooks with ample documentation for

Enhanced Lion Swarm Optimization (ESLO) was used to address fusion from multiple faulty pictures [96]. Also, Improved Neighborhood with Anchored Regression (INAR) was used alongside ensembling to yield viable results [97].	refinement. However, the pseudo-CT images obtained in the above method yielded a PSNR of 29.77 dB and MAE of 92.73 HU [97], performing exceptionally well compared to our defined metrics. Further literature review did not yield any reliable values for SSIM, although could possibly be extrapolated from DICE score and other geometric metrics.	various applications and libraries [98]. There is also documentation provided by Scikit-Learn on the basics of ensemble voting and stacking, along with standard libraries for image processing in Scikit-Image [99].
Concept #5: UNET Architecture		
In addition to being used in the application of pseudo-CT image generation in prior works of literature, the UNET architecture can create highly detailed segmentation maps [100]. 3D U-Nets have been found to achieve the best detail when compared to Atrous-Net and Residual-Net architectures [101]. Variations in U-Net workflow continue to develop including the addition of attention gates, which has shown improvements in the performance of the model in pseudo-CT generation [102].	Comparing existing literature to our initial requirements (*Section #2.2*), this concept meets many of the outline values with great certainty. The generation of pseudo-CT using U-Net architecture in literature clears all of our listed requirements for the proposed solution. This includes PSNR values of around 24 dB, SSIM values of approximately 0.8, MAE values at roughly 100 HU, and a Dice similarity coefficient of 0.94 [102, 103]. No value was ascertained for the SSIM criterion despite thorough research.	U-Net models have become increasingly popular in medical image segmentation processes over the last few years. There exist some open-source models that have been used for application in medical images such as nnU-Net, UNETR, and U-Net in PyTorch [104, 105, 106]. These can provide adequate baselines for further application and development of our model. All of the aforementioned networks are used for image segmentation with medical applications and could therefore be quite beneficial in segregating regions of bone from air and soft tissue.

9. Concept Screening

This section outlines the methodology for quantifiable screening of our initial concepts using the Pugh chart and explicates upon the refined solutions selected for the scoring phase.

9.1. Screening Approach

Machine learning models are extensive, and the concepts listed in the previous section each have further extensions, modifications, and variations to their baseline architecture. Due to the vast number of approaches available, the group decided to split the major concepts aforementioned (*Section 2*) into smaller subdivisions. This was achieved using a Pugh chart to classify the performance of the following methods: GANs, Random Forests, DCNNs, Ensembles UNETs (*Table 15*). The Pugh chart allowed the team to quantify the advantages of each model by comparing them against the evaluation criteria generated earlier (*Sections 2.2, 6.2*). In creating the Pugh charts, each member was assigned one concept to research and find quantitative benchmark values that meet our specifications. Based on the corresponding satisfaction curves, each concept was either categorized as strongly (+), poorly (-), or neutrally (0) satisfying the criteria, as explained by the key (*Table 16*). Additionally, some metrics were not found in literature and thus assigned an NA value. Conclusively, the initial Pugh chart allowed us to narrow down our general, initial concepts into more detailed methods (*Table 15*).

9.2. Pugh Chart for Initial Concepts

Table 15. *Pugh Chart of the Initial Concepts Generated.*

	Concept 1: Generative Adversarial Networks (GAN)	**Concept 2:** Random Forests	**Concept 3:** Deep Convolutional Neural Networks (DCNN)	**Concept 4:** Ensemble Methods	**Concept 5:** UNET Architecture
Criteria 1: Accurate Intensity Distribution (MAE)	0	0	-	-	-
Criteria 2: Peak Signal to Noise Ratio (PSNR)	+	+	+	+	+
Criteria 3: Structure Similarity	+	NA	+	NA	+

Index Measurement (SSIM)					
Criteria 4: DICE Similarity Coefficient (DICE)	0	-	-	-	+
Criteria 5: Spatial Similarity (ASSD)	NA	NA	-	NA	NA
RANK	TIER 1	TIER 3	TIER 3	TIER 2	TIER 1
PASS	YES	NO	NO	YES	YES

Table 16. *Key for the Pugh Chart.*

Symbol	**Meaning**
+	Strongly meets criteria
0	Neutral
-	Poorly meets criteria
NA	No quantifiable data available in literature
TIER 1.	Concept confidently progresses to scoring
TIER 2.	Concept conditionally progresses to scoring
TIER 3.	Concept rejected and excluded from scoring

As described earlier, each concept was assigned a score of positive (+), neutral (0), or negative (-), which articulates how strongly or poorly it fulfills our specifications. Based on metrics obtained from literature, specific values were found for each of the 5 evaluation criteria to determine corresponding customer satisfaction percentages (*Table 17*). A metric was considered to be strongly satisfied if a customer satisfaction of above 66% was achieved, poorly met if the concept had a satisfaction of less than 33%, and neutral otherwise. These percentages were chosen to evenly distribute the percentile ranges among the 3 benchmarks as follows: poor

(0 to 33%), neutral (33 to 66 %), and strong (66 to 100%). For example, the first concept (GAN) has an associated Structure Similarity Index Measure (SSIM) of 0.92, which corresponds to a customer satisfaction of approximately 95% (*Table 17*). This is reflected in the Pugh Chart as strongly meeting the criterion and the cell is assigned a '+' symbol. Kindly note that a value of NA was assigned for metrics that could not be identified from supporting literature.

After filling in the Pugh Chart, our initial concepts were ranked based on different tiers, from #1, strongly meeting the criteria, to #3, barely meeting the criteria. With Concept #1 (GAN) strongly or neutrally meeting all of the criteria, it was ranked as Tier #1 and progressed to subsequent stages of concept generation. Similarly, Concept #5 (UNET), strongly met three of the five criteria, only performing poorly for the MAE metric, and was thus assigned a ranking of Tier #1 as well. Concepts #2, #3 and #4 all had similar results with a combination of poor, neutral, and strong scores. Concept #3 (DCCN) was removed from consideration as there were a greater number of negative (-) than positive (+) markers in the Pugh chart. For the remaining concepts, it was extremely difficult to make a confident pick considering that both had at least two unidentifiable metrics (NA). However, due to its versatility and potential to combine multiple models, concept #4 (Ensembles) was advanced to the next round over Concept #2 (Random Forests), despite the latter having marginally better results. This decision was made following extensive consultation with the client, who agreed with our presented rationale (*Appendix 2-B*). Dr. Lumeng mentioned that there is plenty of freedom for experimentation with this concept, which could potentially lead to improved results based on the choice of models used for the ensembling process. Nonetheless, it must be noted that this screening procedure relied heavily on our selected values for the satisfaction curves. As communicated to us by our client, these numbers may not be fully accurate at this stage of the project and may require some degree of revision in the future based on further research and prototyping. Additionally, although an extensive literature search was performed to identify the best performing networks, data was not available for all 5 criteria which severely weakened our confidence in the outcomes from screening. Keeping in mind these limitations, our team proceeded with refining the concepts.

Table 17. *Summary of Quantitative Performance of Initial Concepts.*

	Concept 1: Generative Adversarial Networks (GAN) [84]	**Concept 2:** Random Forests [87]	**Concept 3:** Deep Convolutional Neural Networks (DCNN) [92]	**Concept 4:** Ensemble Methods [97]	**Concept 5:** UNET Architecture [102]
Criteria 1:	80.23 HU on average for	57.45 HU on average for	79.8 HU on average for	92.73 ± 14.86 HU on	100 HU on average for

Accurate Intensity Distribution (MAE)	head and neck pCT	brain pCT	brain pCT	average for brain pCT	brain pCT
Criteria 2: Peak Signal to Noise Ratio (PSNR)	24 dB	28.33 dB	29.44 dB	29.77 ±1.63 dB	24 dB
Criteria 3: Structure Similarity Index Measurement (SSIM)	0.92	NA	0.95	NA	0.8
Criteria 4: DICE Similarity Coefficient (DICE)	0.86	0.84	0.83 for bone threshold 0.99 for body	0.81 ± 0.03	0.94
Criteria 5: Spatial Similarity (ASSD)	NA	NA	4.59mm on CT 7.58mm on MRI classification	NA	NA

9.3. Most Promising Concepts

Following screening of our general concepts, the team dived deeper into ideation by determining specific models for the Tier #1 (GANs, UNet) and Tier #2 (Ensemble) concepts. Based on our literature search, the most promising refined concepts were identified (*Table 18*)

Table 18. *Summary of Most Promising Refined Concepts.*

Concept #1: Multi-Cycle Generative Adversarial Networks (GANs)
Description: Multi-cycle GANs is a powerful approach that relies on unpaired translation between the generator and discriminator outputs to obtain synthetic CT from MR images. As the name suggests, multiple cyclic losses are accounted for by the model via feedback loops,

which enhances the robustness of the segmentation process. Specifically, a domain-control and pseudo-cycle consistent module is implemented in tandem to add further constraints to the adversarial component of the workflow [88]. By optimizing the synthetic consistencies through each repetition cycle, the resulting performance was significantly better compared to Conventional and Cyclic GANs, as evaluated against key metrics such as MAE and PSNR.

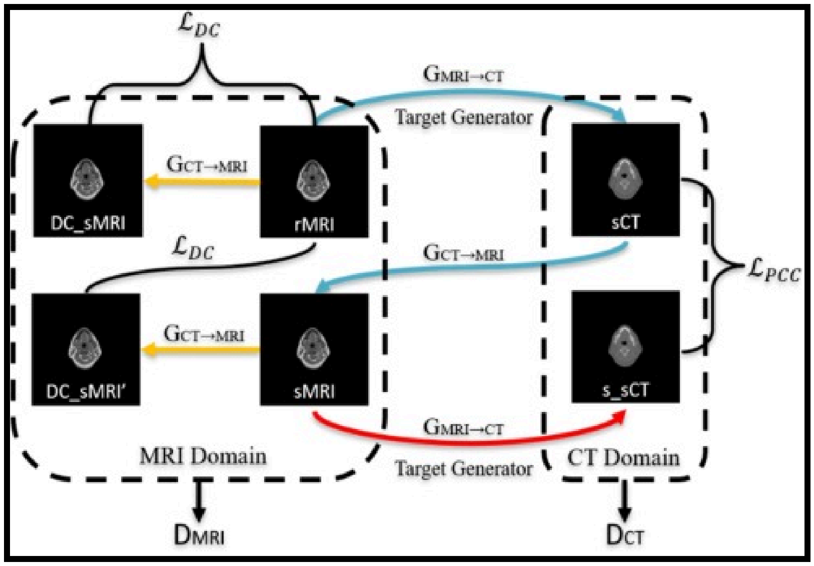


Figure 10. *Concept Flowchart for MRI to CT Conversion via Application of Cyclic Losses. Adapted from Liu Y. et al (2021).*

Concept #2: Stacked Generative Adversarial Networks (sGANs)

Description: Stacked GANs is a promising concept which consists of multiple GANs for generating pseudo CT images. Each GAN used in this method focuses on a specific task from the image conversion process. Hence, the output of one GAN serves as the input for the next GAN [107] and so on. The different nodes could be either conditional or resolution GANs, and are usually quite specific to each task, making the process more accurate and precise [107]. This method has been previously attempted for generating pseudo CT images from ultrasound, with the metrics from that study used for concept screening [107]. Similarly, this approach can be implemented for converting UTE-MRI to pseudo CT by dividing GANs based on key functions such as bias field correction, bone-air segmentation and bone-tissue segmentation. Of particular interest is that this method performed far better than cycleGANs for key requirements such as MAE and the DICE similarity coefficient [107].

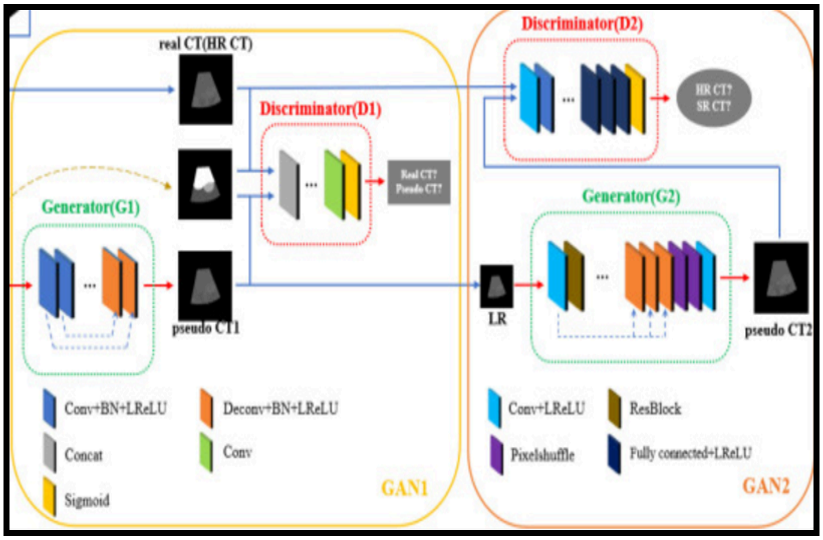


Figure 11. *Concept Flowchart for Pseudo CT Generation with Two Stacked GANs. Adapted from Sun. et al (2021).*

Concept #3: Attention UNet

Description: Attention UNet is based on a traditional UNet model with an added attention gate [100], which allows for a focus on more important features while suppressing irrelevant information. These attention gates are integrated at each level of the network except for the bottleneck. Without adding excessive complexities, this variation can help improve the prototype performance for segmentation, thus making it a suitable model for development of pseudo CT. One study comparing the synthesis of synthetic CT from varying subtypes of traditional UNet architecture found the attention-based model delivered promising results [102].

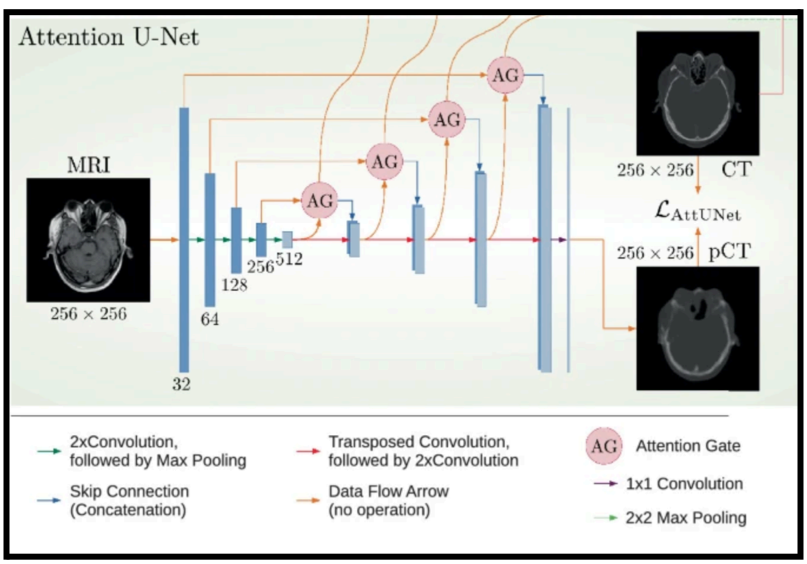


Figure 12. *Concept Flowchart for Pseudo-CT Generation Using Attention U-Net. Adapted from Dovletov G. et al (2023).*

Concept #4: Grad-CAM Guided U-Net (GCG U-Net)
Description: Grad-CAM Guided U-Net integrates a Gradient-Weighted Class Activation Mapping visualization technique into a traditional UNet architecture to improve MRI-to-CT image translation [108]. In particular, this model is able to enhance the synthesis of bone regions within pseudo CT images. There are two components involved in the network: a pre-trained classifier that creates Grad-CAM localization maps and a UNet-based image-to-image translation module. The translation focuses on CT-specific features, such as bone structures, by aligning Grad-CAM heatmaps for pseudo CT images during training. This method improves bone region accuracy and reduces errors across other locations. The results show a decent improvement over traditional UNet architecture. Applications for this model include radiation-free attenuation correction in PET/MRI and MRI-only radiotherapy planning.

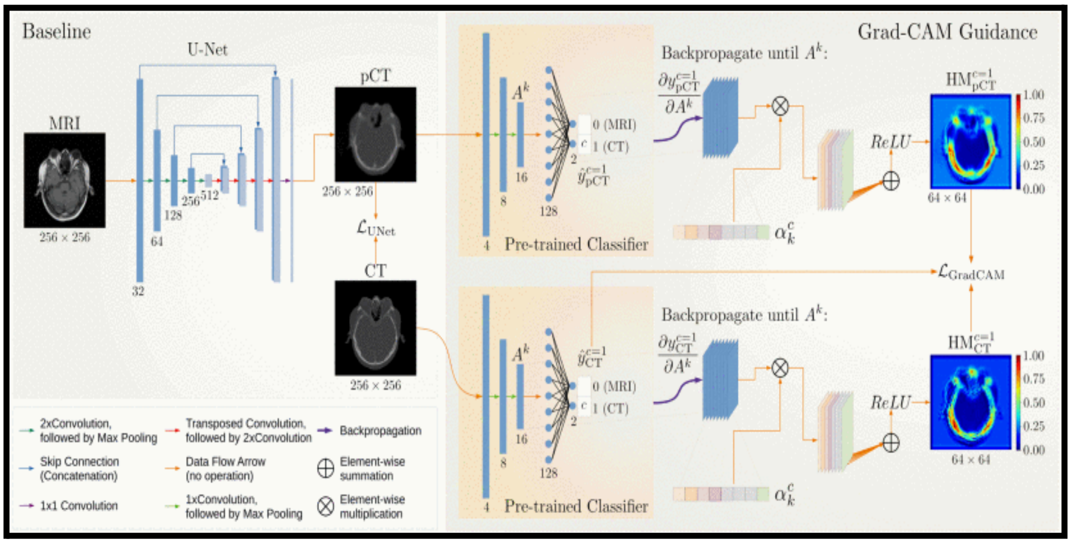


Figure 13. *Concept Flowchart for MRI-Based Pseudo CT Synthesis Using a Grad-CAM Guidance Module (Right) Compared to Baseline U-Net (Left). Adapted from Dovletov G. et al (2022).*

Concept #5: Ensemble Methods
Description: Ensemble methods like multi-regression networks [97], stacked generalization [109], and cascade ensembles of CycleGANs, [110] operate on the core principles of combining many models through voting, averaging, boosting and other functions. This generally results in improved performance over single-model methods in core specifications like MAE, DICE score and PSNR. Instead of treating this concept as an independent entry during scoring, the main motive may be to assess the viability of applying ensembling to high-performing concepts like UNets and Multi-cycle GANs, which is quite well supported by literature. For example, one study adopting cascade ensembles for CycleGANs showed sufficient improvements in MAE, PSNR, and SSIM (38%, 15% and 6%, respectively) [110].

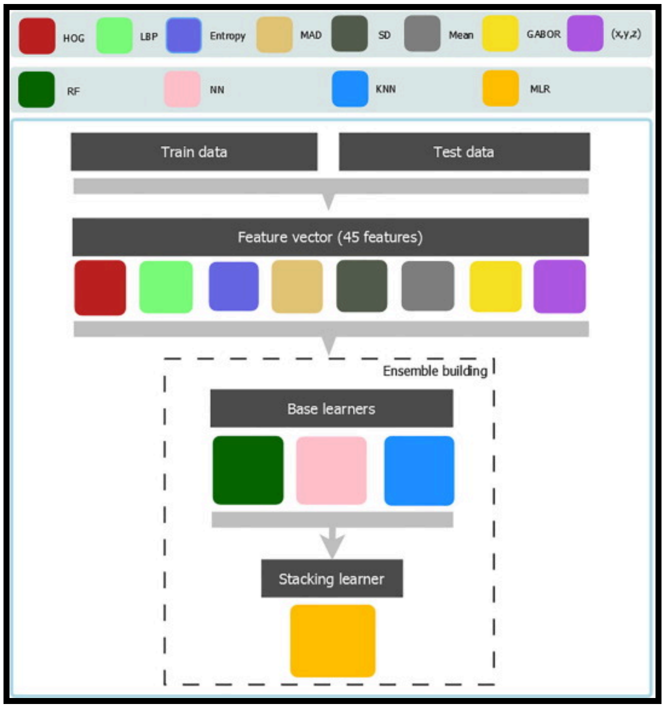


Figure 14. *Concept Flowchart for Pseudo CT Synthesis via Stacked Generalization Ensemble. Adapted from Boukellouz and Moussaoui (2021).*

9.4. Pugh Chart for Refined Concepts

After conducting a literature review for the refined concepts, the quantitative performance of each method was mapped against the evaluation criteria using a Pugh chart. As mentioned previously (*Section 9.1*), the same process ranking of the initial concepts was repeated, with each method given a score of positive (+), neutral (0), or negative (-). Customer satisfaction of above 66% was assigned as having strongly met the criterion while, a satisfaction of less than 33% indicated that the concept poorly met the criterion, with neutral given the range of values in between. The Pugh chart for the iterated concepts is provided below (*Table 19*).

Table 19. *Pugh Chart of the Refined Concepts.*

	Concept 1: Multi-Cycle Generative Adversarial Networks	**Concept 2:** Stacked GANs	**Concept 3:** Attention U-Nets	**Concept 4:** Grad-CAM Guided U-Net	**Concept 5:** Ensemble Methods

Criteria 1: Accurate Intensity Distribution (MAE)	+	+	0	0	0
Criteria 2: Peak Signal to Noise Ratio (PSNR)	+	NA	+	+	+
Criteria 3: Structure Similarity Index Measurement (SSIM)	+	NA	+	+	+
Criteria 4: DICE Similarity Coefficient (DICE)	+	0	NA	-	0
Criteria 5: Spatial Similarity (ASSD)	NA	NA	NA	NA	NA
RANK	TIER 1	TIER 3	TIER 3	TIER 3	TIER 2
PASS	YES	NO	NO	YES	YES

Following rating of the concepts as strongly, poorly, or neutrally meeting the associated criteria, each method was assigned a ranking, with Tier #1 being the most promising and Tier #3 being the least enticing approach. Concept #1 (Multi-cycle GANs) meets almost all of the criteria strongly, and was thus given a Tier #1 rank. Meanwhile, concept #5 (Ensemble Methods) was ranked as Tier #2 since there were no negative (-) markers in its column for the Pugh chart. As previously explained, this method holds immense potential for combination of different models as was correspondingly retained for scoring. Concepts #2, #3, and #4, were all given a rank of Tier #3. For Concept #2 (Stacked GANs), the lack of substantial literature on this topic and few available metrics for quantification signified that it would no longer be considered for further consideration (*Table 20*). Concept #3 (Attention U-Net) and Concept #4 (Grad-CAM Guided U-Net), overall performed quite similarly and worse than the other methods. However, Concept #4 was selected over Concept #3 as it achieved marginally better scores on the criteria with higher weights (PSNR, SSIM, DICE). The team proceeded with a final round of scoring following approval from the client on the aforementioned chosen concepts (Appendix 3-B).

Table 20. *Summary of Quantitative Performance of Refined Concepts.*

	Concept 1: Multi-Cycle Generative Adversarial Networks [84]	**Concept 2:** Stacked GANs [107]	**Concept 3:** Attention U-Nets [102]	**Concept 4:** Grad-CAM Guided U-Net [108]	**Concept 5:** Ensemble Methods [97]
Criteria 1: Accurate Intensity Distribution (MAE)	75.7 ± 14.6	66.36 ± 1.85	99 ± 32	96 ± 34	92.73 ± 14.86
Criteria 2: Peak Signal to Noise Ratio (PSNR)	29.1 ± 1.6	NA	24.5 ± 1.6	25.0 ± 2.1	29.77 ± 1.63
Criteria 3: Structure Similarity Index Measurement (SSIM)	0.92 ± 0.02	NA	0.801 ± 0.059	0.806 ± 0.067	0.89 ± 0.01 []
Criteria 4: DICE Similarity Coefficient (DICE)	0.86 ± 0.03	0.902 ± 0.015	NA	0.667± 0.09	0.87 ± 0.03
Criteria 5:	NA	NA	NA	NA	NA

Spatial Similarity (ASSD)					

10. Concept Scoring

This section outlines the approach to classify our final concepts for deep learning-based segmentation, which involved constructing multiple Weighted Decision Matrices.

10.1. Scoring Approach

Comparison between our 3 final concepts was achieved through Weighted Decision Matrices (*Tables 21, 22, 23*) based on the respective weights for our previously defined evaluation criteria (*Section 2.2, 6.3*). However, the Average Symmetric Surface Distance (ASSD) criterion was removed from the list as none of the 3 concepts had supporting metrics from academic literature. As a result, weights were redistributed among the remaining 4 criteria by dividing the original values (*Table 15*) from the total of the remaining weights, which was 0.75. This allowed us to scale up our weights, ensuring that the total added up to 1 for consistency.

Afterward, each criterion was assigned a rating based on how well the concept met the specifications; with 3 as ideal, 2 being nearly ideal, and 1 as not ideal. Each criterion's weight was then multiplied by its ranking to obtain a score, which was summed up across all criteria for a total out of 3. Based on each concept's final score, a final ranked list was generated in order to determine our primary concept(s) for the deep learning-based synthesis (*Table 24*).

10.2. Weighted Decision Matrices for Final Concepts

Table 21. *Weighted Decision Matrix for Final Concept 1.*

Concept 1: Multi-Cycle Generative Adversarial Networks (GANs)				
	Weight	**Rating**	**Comments**	**Score**
Criteria 1: Accurate Intensity Distribution (MAE)	0.134	3	The MAE value for multi-cycle GANs was found to be 75.7 ± 14.6 [84]. This was the lowest MAE score when compared to the other two concepts and was thereby assigned a high rating of 3.	0.402

Criteria 2: Peak Signal to Noise Ratio (PSNR)	0.20	3	The PSNR value for the concept of Multi-Cycle GANs was 29.1 ± 1.6 dB according to the research paper [84]. This metric generated a very high satisfaction score of approximately 96%.	0.60
Criteria 3: Structure Similarity Index Measurement (SSIM)	0.333	3	The SSIM value for multi-cycle GANs was found to be 0.92 ± 0.02 [84]. This value generates a satisfaction of approximately 95%, which was the highest when compared to the other two concepts.	0.666
Criteria 4: DICE Similarity Coefficient (DICE)	0.333	1	The DICE similarity coefficient for this concept was determined to be 0.86 ± 0.03 [84]. This metric would generate a satisfaction score of 30% based on our curves for the evaluation criterion, and was thus given the lowest rating.	0.333
SCORE				**2.334**

Table 22. *Weighted Decision Matrix for Final Concept 2.*

Concept 2: Grad-CAM Guided U-Net				
	Weight	**Rating**	**Comments**	**Score**
Criteria 1: Accurate Intensity Distribution (MAE)	0.134	1	A MAE value of 96 ± 34 was obtained, which corresponded to approximately 60% satisfaction for this evaluation criterion [108]. This was the highest value out of all 3 concepts, and was therefore assigned a rating of 1.	0.134
Criteria 2: Peak Signal to Noise Ratio (PSNR)	0.20	3	A PSNR value of 25.0 ± 2.1 dB was found in literature [108]. When evaluating this metric against the criterion, a customer satisfaction of approximately 80% was achieved. With this satisfaction percentage being relatively high, a ranking of 3 was chosen in this case.	0.60
Criteria 3: Structure	0.333	3	Grad-CAM Guided U-Net was found to have an SSIM value of 0.806 ± 0.067 [108]. Measuring this against the	0.999

Similarity Index Measurement (SSIM)			evaluation criteria we obtain a customer satisfaction of 80%. Similar to the second criterion, a ranking of 3 was given due to its high satisfaction percentage (above 66%).	
Criteria 4: DICE Similarity Coefficient (DICE)	0.333	1	A DICE similarity coefficient of 0.667 ± 0.09 was found in literature [108]. This performs quite poorly when measured against our evaluation criterion and was therefore assigned a ranking of 1.	0.333
SCORE				**2.066**

Table 23. *Weighted Decision Matrix for Final Concept 3.*

Concept 3: Ensemble Methods				
	Weight	**Rating**	**Comments**	**Score**
Criteria 1: Accurate Intensity Distribution (MAE)	0.134	2	92.73 ± 14.86 was found to be the common range of MAE after literature review, which falls in the middle range for satisfaction [97].	0.268
Criteria 2: Peak Signal to Noise Ratio (PSNR)	0.20	3	Similarly, a 29.77 ± 1.63 dB was determined, which indicated that the model performed strongly against this evaluation criterion [97].	0.60
Criteria 3: Structure Similarity Index Measurement (SSIM)	0.333	3	A cascade ensemble study provided SSIM values of 0.90 ± 0.01, which was a slight improvement when applied to the cycleGAN architecture in the same study [110]. According to our previously outlined metrics, this number places the concept in the top percentiles.	0.999
Criteria 4: DICE Similarity Coefficient (DICE)	0.333	1	0.87 ± 0.03 was reported as the value for the evaluation criterion in a research paper by Zhong et al [97]. This measurement coincided with a low score relative to the other concepts.	0.666

SCORE		2.20

10.3. Ranked List of Final Concepts

After constructing the Weighted Decision Matrices for each of our top three concepts, a final ranking was obtained based on the scores computed in the previous section (*Table 24*).

Table 24. *Ranked List of Final Concepts for Deep Learning Synthesis.*

Rank	Concept	WDM Score	Commentary
1.	Multi-Cycle Generative Adversarial Networks (GANs)	2.334	This design scored the highest amongst the 3 final concepts and would thus be selected as our primary approach for the deep learning- based synthesis. Multi-cycle GANs scored the highest for 3 out of the 4 criteria assessed: MAE, PSNR and SSIM, while performing poorly on the DICE, which had the highest weight of 0.33. Regardless, this concept finished first and would therefore be pursued for our image segmentation workflow. Based on our recent literature review, multi-cycle GANs is an extremely promising concept that showcases a lot of potential for integration within our prototype [111].
2.	Ensemble Methods	2.20	This design scored neither the highest nor the lowest amongst the 3 final concepts. The ensemble methods performed well on the PSNR and MAE criteria, neutral on the MAE, and quite poorly on the DICE, which was weighted the highest [97, 110]. Hence, it finished behind the GANs in our ranking. As an ensemble is essentially a combination of different models, we could potentially experiment with a GAN-UNET network for pseudo CT generation from MR images. Ergo, this is a suitable secondary concept for the prototyping phase.
3.	Grad-CAM Guided U-Net	2.066	This method scored the lowest out of the 3 final concepts as it obtained the smallest rank for 2 of the 4 criteria: PSNR and SSIM. However, it did perform quite well on the DICE score and MAE. Although this concept was ranked the lowest, recent literature has suggested that U-Nets are also quite capable of enhancing synthesis of bone regions for pseudo-CT images [108]. Additionally, this was a concept specifically mentioned by the client (Appendix 2-C). Therefore, this solution could still be reasonably explored for integration into our imaging prototype.

BMEG 457 – Design History File (DHF) 4.

December 06, 2024

Client: Siemens Healthcare Ltd. (Siemens Healthineers Canada)

Project: Magnetic Resonance Imaging (MRI)-Based Pseudo Computed Tomography (pCT) Generation Using Ultrashort Echo Time (UTE) Technique

Team #17: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen

Faculty Supervisor: Tim Salcudean

Report Type: Critical Function Prototype

Section Word Count: 1382

Abstract

The following document presents our Critical Function Prototype (CFP) based on determinative elements identified in the Function Structure Diagram (*Section 7*), as well as the testing framework for validation. The presentation was also accompanied by a demonstration of our design through code (OpenCV, NumPy) and imaging software (3D Slicer), respectively.

BMEG 457 – Design History File (DHF) 5.

April 11, 2025

Client: Siemens Healthcare Ltd. (Siemens Healthineers Canada)

Project: Magnetic Resonance Imaging (MRI)-Based Pseudo Computed Tomography (pCT) Generation Using Ultrashort Echo Time (UTE) Technique

Team #17: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen

Faculty Supervisor: Tim Salcudean

Report Type: Technical Analysis

Word Count: 1792

Abstract

The following document outlines the analytical approach undertaken to iteratively refine the design modules based on identification of its key parameters. Further, the report highlights the different optimization methods which were experimented with to yield the most convincing results for the inverse-logarithmic scaling, bias correction, and automatic thresholding functions.

IX. *Table of Contents*

X. *List of Tables & Figures*

11. *Technical Analysis Plan*

This section outlines our approach for the subsequent technical analysis and automated image prototyping. The team identified key design variables for optimization, proposed the methodology for parameter modification, specified performance metrics for quantification, and created a workplan for task delegation amongst group members with a timeline for completion.

11.1. *Design Parameters*

1. Bias correction for improved image uniformity.
2. Automation of threshold selection for anatomical segmentation.

11.2. *Proposed Methodology*

1. The histogram generated from an inverse-logarithmic scaled image was utilized for bias correction, with the focus being on identifying two major peaks for soft tissue and background. Alternatively, an N4ITK-based method focusing on hyperparameter tuning was also implemented to determine the optimal technique for bias correction.
2. The performance of the imaging module would be evaluated based on the generated histogram and image after bias correction. This involves manual visualization of the selected thresholds on the Gaussian-fitted histogram of the image. The signal should have two peaks, with the first representing the soft-tissue signal and the second representing noise. The bone region will be represented as the flat layer between these two signals. A more prominent definition of the soft-tissue and noise peak corresponds to better performance of the automated functions.

11.3. *Outcomes*

1. Comparative analysis of the histograms generated following bias correction performed worse than the N4ITK hyperparameter optimization method.
2. An automated threshold selection was implemented, and it worked well on signals with a narrow full width of half-maximum (FWHM). Further refinement is needed to improve segmentation performance on signals with a wider FWHM.

11.4. *Work Plan*

The following page provides an outline of tasks with assigned members for completion (*Table 25*). Additionally, a Gantt Chart is included that provides a timeline to streamline the prototyping across Development Phases #1,#2, and #3 (*Figure 15*). Resource Planning, Testing and Validation are also integrated to ensure timeliness and quality of deliverables, with the intent of leaving ample room for client and instructor feedback prior to Design & Innovation Day.

Table 25. *Delegation of Tasks Amongst Team Members*

No.	Task	Description	Assigned Member(s)
Development Phase #1.	Bias Correction	Use the N4ITK module to reduce signal inhomogeneities in the UTE-MR image before rescaling.	Aly Khan Nuruddin, Lynn Alvarez Krautzig
	Manual Thresholding	Utilize the histograms generated to visually detect and input the threshold parameter values.	Yuheng Zhang
	Image Segmentation	Obtain the corrected pseudo-CT image with differentiated soft tissue, bone and noise signals.	Jackson Chen, Manan Verma
Development Phase #2.	Hyperparameter Optimization	Experiment with parameters for the SimpleITK module to yield an improved, bias-corrected image.	Jackson Chen, Manan Verma, Yuheng Zhang
	Automated Thresholding	Implement a histogram-based approach for automated threshold selection via Gaussian fitting.	Aly Khan Nuruddin, Lynn Alvarez Krautzig
	Image Segmentation	Obtain the corrected pseudo-CT image with differentiated soft tissue, bone and noise signals.	Lynn Alvarez Krautzig
Development Phase #3.	Deep Learning Training	Train a UNet architecture and Multi-cycle GAN model based on provided datasets from the client.	Lynn Alvarez Krautzig, Manan Verma (UNet) Aly Khan Nuruddin, Jackson Chen, Yuheng Zhang (GAN)
	Model Refinement	Improve algorithm performance based on iterative feedback with possible integration of ensembles.	

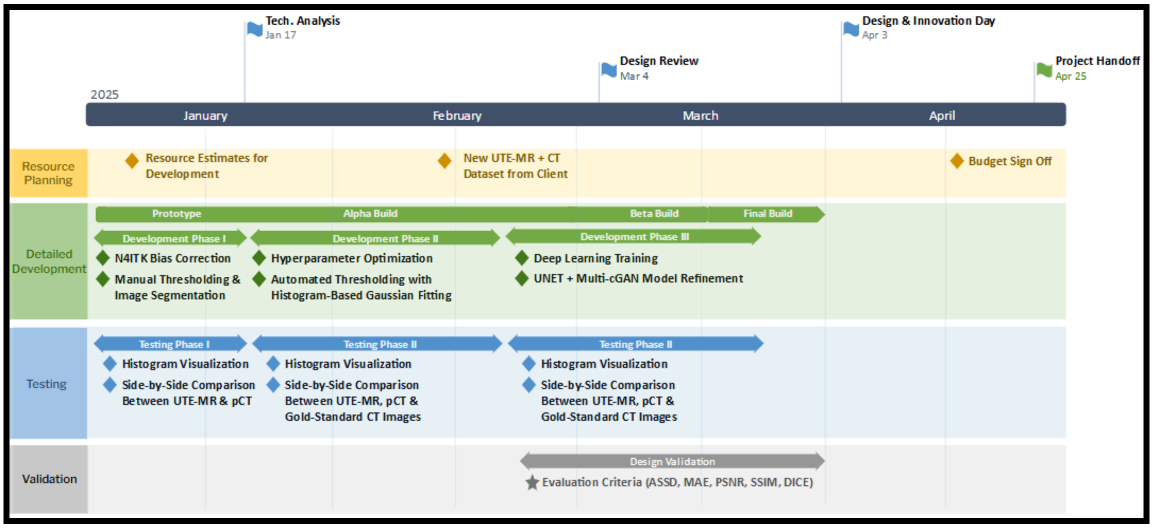


Figure 15. *Gantt Chart with Proposed Timeline for Development.*

12. Analysis Report

This section summarizes the experiments and findings from our technical analysis. We document our aims regarding the testable design parameters, describe our methodological approach, present key results, discuss the implications and limitations of our findings, as well as provide clear recommendations for holistic integration within our final prototype design.

12.1. Histogram-based Bias Correction

Aims:

To implement a histogram-based bias correction method for improved image uniformity and accurate segmentation. In the previous version of our workflow, the N4ITK bias correction method was utilized. However, based on feedback from our client, we were encouraged to implement and analyze the histogram-based bias correction method for potentially better results.

Methods:

This approach involves utilizing the histogram obtained from the inverse-logarithmic scaled image for identification of the two major peaks which correspond to soft tissue (left) and background (right), as shown below (*Table #26*).

Results:

The comparative analysis of the two methods for bias correction, which are N4ITK and histogram-based, is documented (*Table #27*). The histogram-based bias correction indicates a shorter and wider left peak for the soft tissue compared to the N4ITK method. Since a narrower peak is desired for the soft-tissue and air, the N4ITK method provided the better results.

Table 26. *N4ITK and Histogram-Based Bias Correction Output Comparison.*

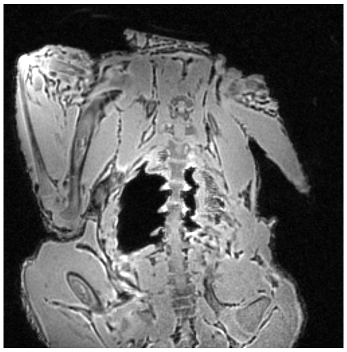
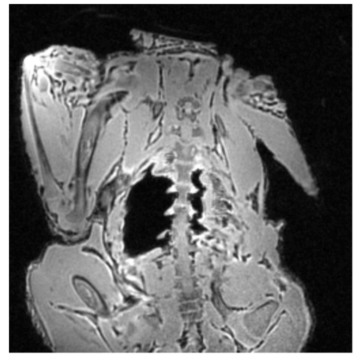
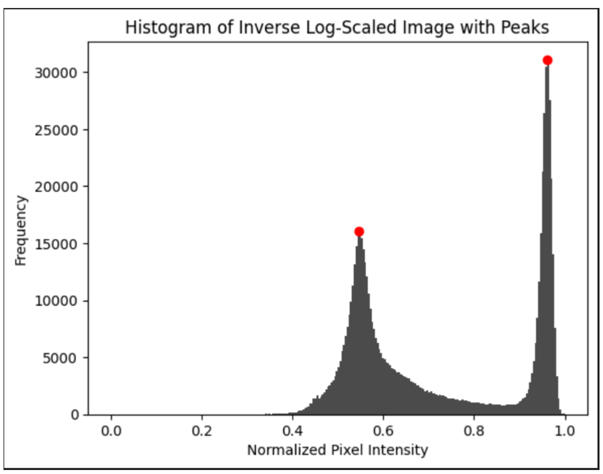
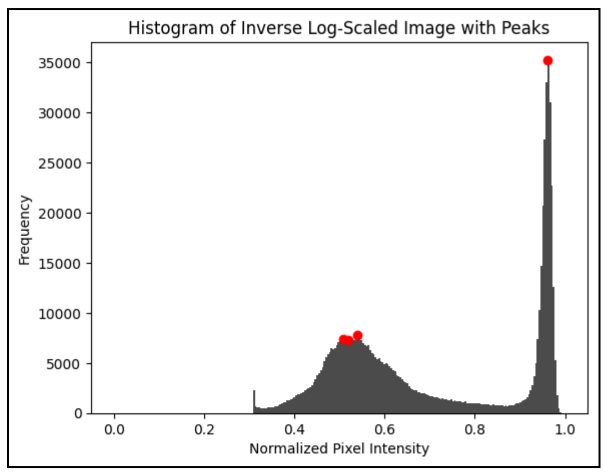
N4ITK Bias Correction	Histogram-Based Bias Correction
	

Table 27. *N4ITK and Histogram-Based Bias Correction Graphical Comparison.*

N4ITK Bias Correction	Histogram-Based Bias Correction
	

Discussion:

The histogram-based bias correction approach did not perform better than the N4ITK-based method from the comparative analysis of the two peaks. Hence, we can conclude that the N4ITK module yields more uniform intensity distributions and better soft tissue contrast.

Recommendations:

Using the histogram-based bias correction as an additional step to the N4ITK method may help further refine intensity normalization, especially in regions where N4ITK alone may leave residual bias. The combination of both methods may provide an improved histogram with narrower and sharper soft tissue peaks, indicating better bias correction. Another possible approach for improving the image quality would involve hyperparameter optimization for the N4ITK module. This would allow for fine-tuning and likely provide nominal improvements.

12.2. Automatic Thresholding

Aims:

An automatic threshold selection was implemented using the improved bias correction filter with pre-selected parameters. In the previous iteration of our workflow, we manually inputted the threshold values to do segmentation. Ideally, as indicated by our client, this process would be automated for rapid, more efficient generation of segmented pCT images. Thus, not requiring manual thresholds from users would speed up downstream computation significantly.

Methods:

Gaussian fitting of the data's histogram allows for the calculation of the Full-Width Half Maximum (FWHM) for both the signal (left) and noise (right) peaks. Initially, threshold selection was attempted without Gaussian fitting but obtaining consistent results was challenging. Hence, threshold selection was calculated using the following formula provided by Wiesinger et al. (2015) [112] (*Equation 1.*):

$$[center\ (signal)\ +\ 2\ *\ FWHM(signal),\ center(noise)\ -\ 2\ *\ FWHM\ (noise)]$$

Equation 1: *FWHM Computation*

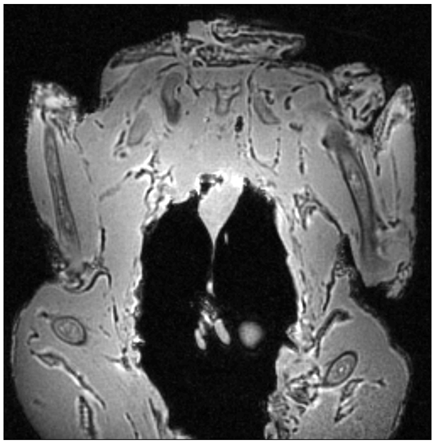
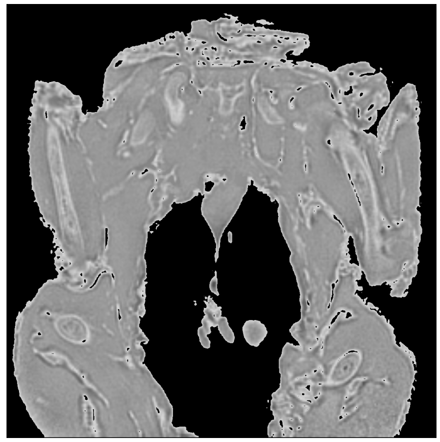
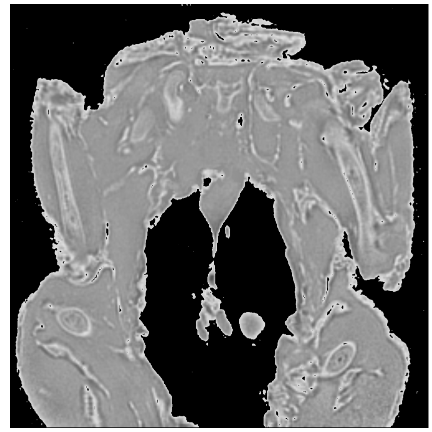
The robustness of this automated thresholding was tested on images of the chicken UTE-MRI data provided by our client, Dr. Lumeng Cui, from Siemens Healthineers.

Results:

The images below outline the results obtained using the manual thresholding used in the previous workflow alongside the images from the automatic thresholding process (*Table #28*).

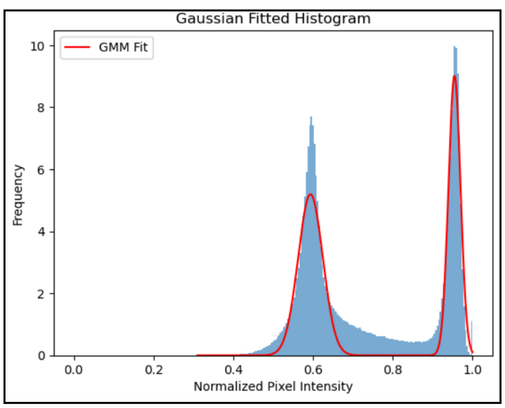
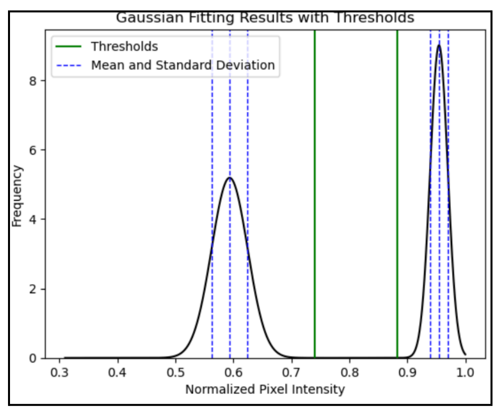
Table 28. *Comparison of Manual vs. Automatic Thresholding for Chicken*

Original Image	Segmented Image with Manual Thresholding	Segmented Image with Automatic Thresholding

The histograms below show the Gaussian fitting results as well as the thresholds automatically selected using the defined formula on the previous page (*Table #29*).

Table 29. *Gaussian Fitting Results of Chicken Image.*

Gaussian Fitting	Gaussian Fitting with Thresholds
	

<u>*Discussion:*</u>

The automatic thresholding module may not be fully applicable for the final iteration of our design, largely depending on the selected segmentation methods used. Our current differentiation approach utilizes histograms to segment air, soft tissue, and bone regions from MR images, which would be suitable for automatic thresholding. However, a limitation of this approach is the dependence of the threshold value on the signal FWHM. The results below outline the performance of the algorithm on a different slice of the MRI corresponding to the shoulder. Due to the wide FWHM of the first peak, the thresholds obtained are quite narrow.

Table 30. *Segmentation Comparison of Manual vs. Automatic Thresholding for Shoulder*

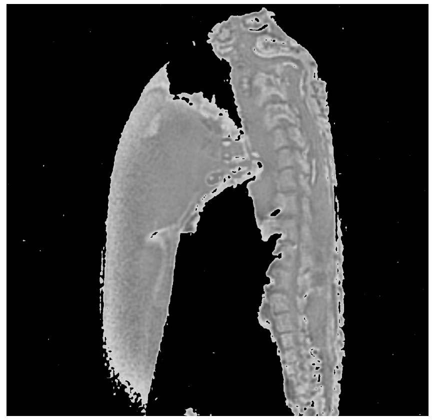
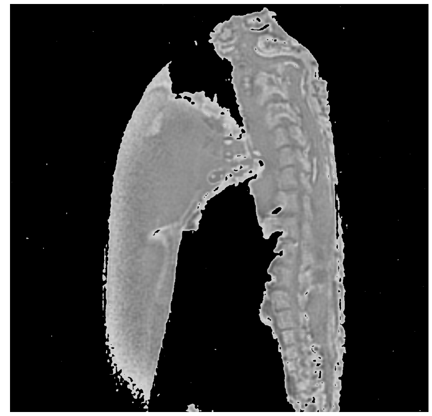
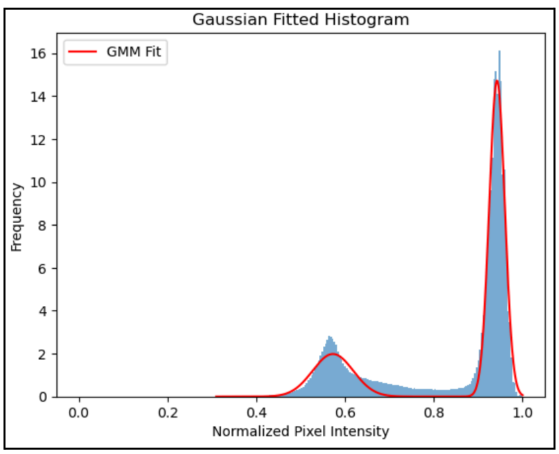
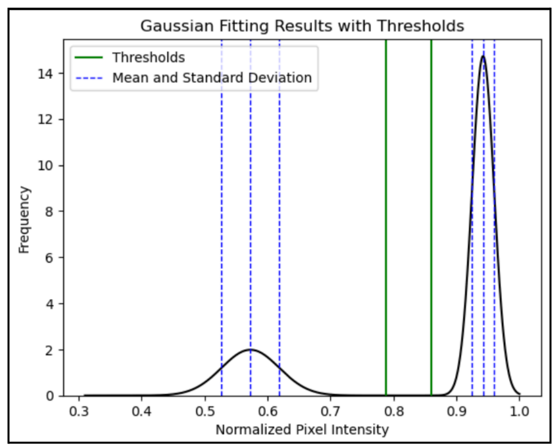
Original Image	Manual Thresholding	Automatic Thresholding
		

Table 31. *Gaussian Fitting Results of Shoulder Image*

<table>
<tr><th>Gaussian Fitting Results</th><th>Gaussian Fitting Results with Thresholds</th></tr>
<tr><td>


</td><td>


</td></tr>
</table>

<u>*Recommendations:*</u>

Ideally, the client would prefer the workflow to be automated and to require minimal user input. However, the accuracy of this automated thresholding workflow heavily depends on the FWHM of the first signal peak. As a result, this automation is reliant on previous signal processing steps. Hence, for further algorithm iterations, we will use automated thresholding sparingly and as needed based on the defined use case, while refining other processing steps.

12.3 N4ITK Hyperparameter Optimization

<u>*Aims:*</u>

The goal of hyperparameter optimization for the N4ITK module is to improve the accuracy and effectiveness for bias-field correction.

Methods:

The implementation involved independently changing the 4 default hyperparameters for the N4ITK module: SetSplineOrder, SetConvergenceThreshold, SetNumberOfHistogramBins and SetMaximumNumberOfIterations, while keeping the others constant [113]. A full range of values were tested for each of the hyperparameters and the histogram from each of the modifications was observed to identify the best series of combinations.

A study titled *"A Segmentation Based Method Improving N4ITK Performance"* by Dovrou et al. (2023) systematically evaluated various parameter settings of the N4ITK bias field correction algorithm to optimize its performance [114]. Key parameters tested include:

- *Convergence threshold*: Determines stopping criterion for the iterative bias field estimation
- *Shrink factor*: Controls the level of image downsampling to reduce complexity
- *Number of fitting levels*: Affects the resolution of the B-spline grid across iterations;
- *Number of iterations allowed per level*.

Additionally, the use of a binary mask was examined, where the algorithm either used a provided mask or defaulted to non-zero voxels for bias field estimation. The optimal configuration was identified based on the filter setting that yielded the minimum full width at half maximum (FWHM), indicating a more homogeneous intensity distribution.

Results:

The results indicate that the combination of optimal hyperparameters provided an image with ~70-80% improvement in contrast flattening (*Table #32*). Also, there is significant visual improvement in the bias correction compared to the default hyperparameters, with sharper, more prominent signals observed. Further, the histogram of the new hyperparameters showcase better results as indicated by the narrower and sharper soft-tissue peak (left) (*Table #33*).

Table 32. *N4ITK/Bias Correction Histogram Comparison for New Hyperparameters*

Original Image	Bias Correction with Default Hyperparameters	Bias Correction with Optimal Hyperparameters

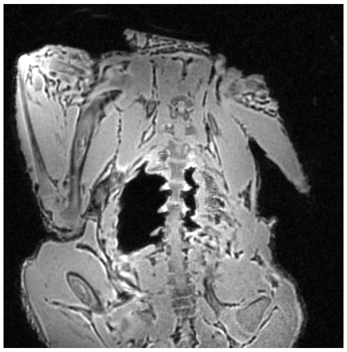
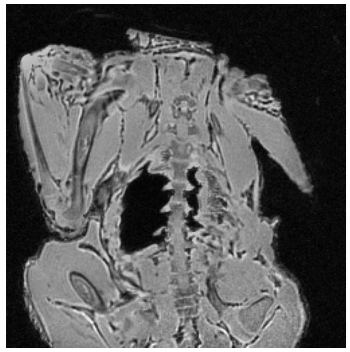
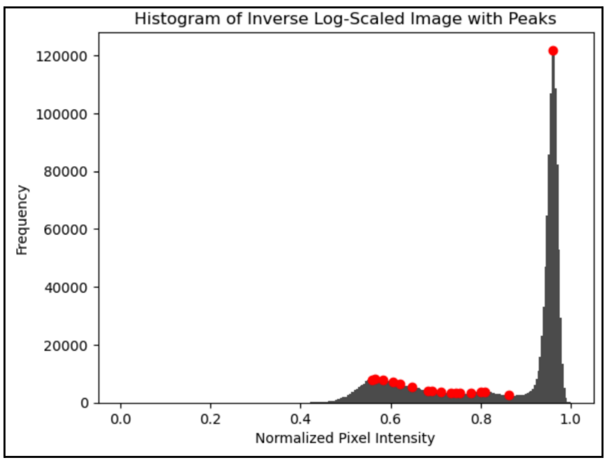
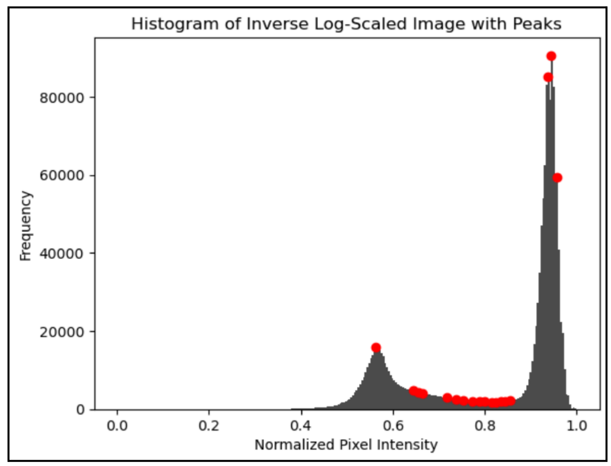
		

Table 33. *Comparison of Old vs. New Histogram for Bias Correction*

Default Hyperparameters	Optimal Hyperparameters
	

Discussion:

The results demonstrate that hyperparameter optimization significantly enhances the performance of the N4ITK bias-field correction method. Adjusting key parameters such as SetSplineOrder, SetConvergenceThreshold, SetNumberOfHistogramBins, and SetMaximumNumberOfIterations, provided a notable improvement in image uniformity and soft-tissue contrast. Subsequently, this technique would be retained for future iterations.

Recommendations:

A potential method for further analysis of ideal hyperparameters would involve a quantitative comparison of results following different combinations. A grid-based search algorithm could be implemented to statistically determine the best set of values. This could provide deeper insights into the relative contributions of each hyperparameter to the output. Additionally, the tweaking of hyperparameters based on specific regions in the input UTE-MR image could also be investigated to find out which ones are most effective for different anatomical representations. Possible exploration of hyperparameters beyond the four primary ones listed previously could also be looked into to further refine the bias correction performance.

BMEG 457 – Design History File (DHF) 6.

April 11, 2025

Client: Siemens Healthcare Ltd. (Siemens Healthineers Canada)

Project: Magnetic Resonance Imaging (MRI)-Based Pseudo Computed Tomography (pCT) Generation Using Ultrashort Echo Time (UTE) Technique

Team #17: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen

Faculty Supervisor: Tim Salcudean

Report Type: Design Review

Word Count: 1437

Abstract

The following document quantifies the risk level of possible failure modes within the design, proposing strategies to mitigate the most critical functions. Additionally, the report explores the environmental impacts of the image processing prototype via a complete, life-cycle assessment. Lastly, the updated needs, requirements, and evaluation criteria are summarized and tabulated.

XI. *Table of Contents*

XII. *List of Tables & Figures*

14. Fault Tree Analysis

In this section, our team conducted a comprehensive analysis of potential failure modes within the image processing prototype using a Fault Tree Analysis (FTA). The group created a detailed diagram identifying critical failure points and developed specific mitigation strategies (*Figure #16*). These insights informed several modifications and updates to our specifications.

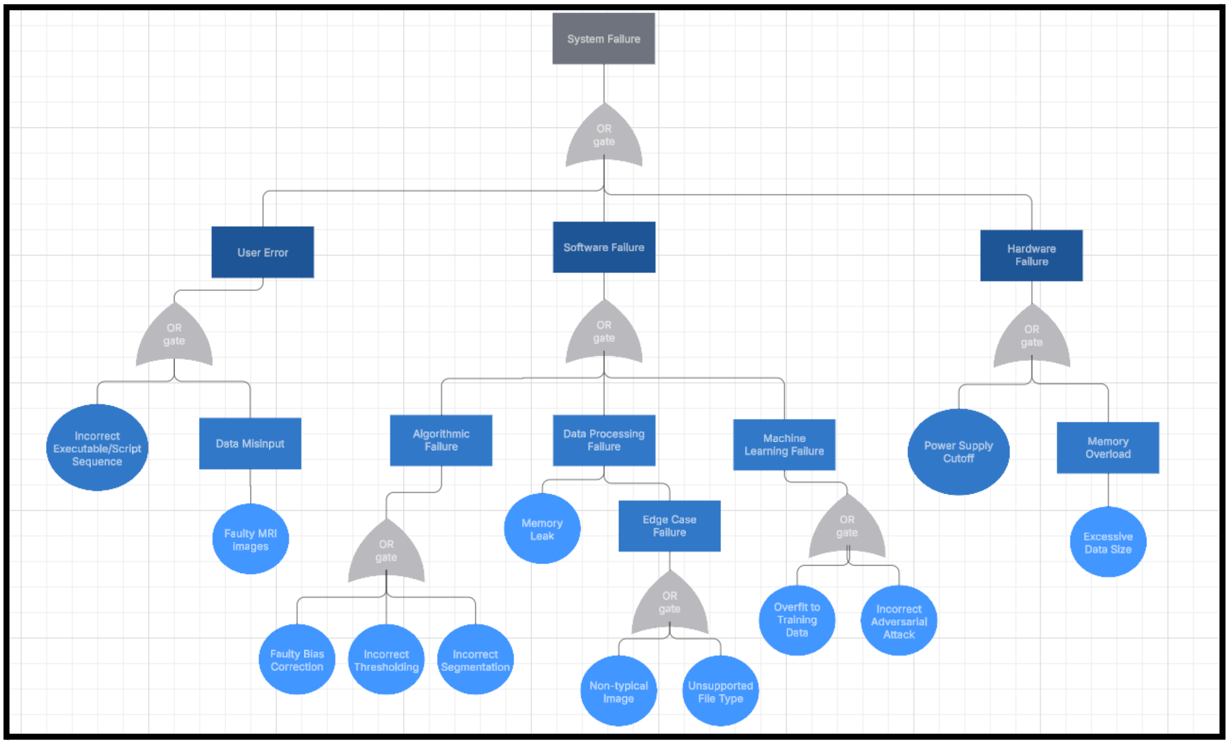


Figure 16. *Fault Tree Analysis of our MRI to Pseudo-CT Processing Pipeline*

14.1. Justification

Our processing pipeline for conversion of MRI to pseudo-CT images is better suited for a Fault Tree Analysis (FTA) over a Failure Modes and Effects Analysis (FMEA). This is primarily because our system's potential failure points are hierarchical and concurrent in nature. An FMEA focuses on identifying individual failure modes and their effects in isolation. On the other hand, an FTA focuses on analyzing and structuring failure pathways as combinations of events. This approach was more realistic given the complexity of our processing workflow. At every stage, there are potential component failures. This can be observed by the abundance of OR gates within our FTA diagram, thereby reflecting interdependence between the different events.

The Head Teaching Assistant (TA), Fraser Douglas, pointed out that the FTA would allow us to better visualize the contributions of singular events to the whole system failure (see *Appendix 6-A*). Overall, using an FTA will ensure that our pipeline remains robust despite cascading failures like user misinputs, algorithmic miscalculations, and hardware constraints. Hence, a clearer representation of such modular mishaps would help us prioritize critical risks and make strategic improvements to minimize the likelihood of system failure.

14.2. Conclusions and Recommendations

After constructing our FTA diagram (*Figure #16*), we recommend implementing numerous workflow enhancements to prevent potential failure points in our processing pipeline.

First, user error remains a significant source of failure. There may be few isolated cases where images not corresponding to UTE-MR are added as inputs to the system. Our group suggests integrating automated image verification with preprocessing checks to cover such edge cases so only valid MRI scans are accepted into the pipeline. In the case of faulty input, a messaging system will be used to clearly display the error to users. Additionally, algorithmic failures related to faulty bias correction, thresholding, and segmentation can be mitigated by fine-tuning parameters and validation against diverse datasets. Doing so will drastically reduce the likelihood of processing errors and improve the overall robustness of our workflow.

Another critical area for improvement is memory management. For image processing pipelines in general, memory leaks and excessive data sizes can pose a risk to system stability, leading to processing failures or crashes. To mitigate that risk, we propose optimized memory allocation techniques such as garbage collection and dynamic resource allocation based on input size. A monitoring system could also be implemented to detect abnormal memory usage patterns, thus addressing potential issues before system failure. Applying these safeguards will maximize the efficiency and stability of our pipeline across local and cloud-based compute environments.

Given the reliance on machine learning models in our workflow, we also recommend strengthening training and validation methods to prevent failures due to overfitting. This can be achieved by diversifying training datasets and incorporating k-fold cross-validation [115]. We may also consider ensemble methods and model hardening techniques to combat adversarial attacks [116]. Lastly, to reduce the environmental footprint of our device and to prevent potential power supply cutoffs, our resource usage will be optimized by improving the efficiency of our machine learning pipeline, thereby possibly lowering any hardware requirements.

Overall, our FTA diagram has provided us with an extensive roadmap for implementation of safeguards to address critical failure points. By considering the above recommendations, we can enhance the reliability and efficiency of our MRI-to-pCT conversion pipeline.

15. Life Cycle Assessment

This section evaluates the environmental impacts across our design's lifecycle. The tabulated information below analyzes the ecological footprint of our device during manufacturing, operation, and end-of-life stages. Further, each process is evaluated and ranked in terms of its impact, followed by identification of factors within the engineering team's domain. Our team also conducted a comparison of the energy consumption for a regular non-AI pCT pipeline with a deep learning approach, against the control, which is a standard CT-scan.

15.1. Identifying Design Stages

Table 34. *Environmental Impact Ranking of Manufacturing*

Raw Material Acquisition/Manufacturing				
ID	**Item**	**Environmental Impact Rank**	**Notes**	**Controllable?**
1	Computational Hardware	1	The environmental impact based on energy consumption would depend on whether the algorithm runs on high performing GPUs.	Yes

Table 35. *Environmental Impact Ranking of Operations*

Operation/Use/Maintenance				
ID	**Item**	**Environmental Impact Rank**	**Notes**	**Controllable?**
1	Computational Cost for Algorithm	1	Running the preprocessing pipeline on hardware would require processing power, which would be high since the algorithm deals with processing and translation of multi-slice MR images.	Yes
2	Model Training	2	Training a deep learning model can significantly increase energy consumption based on the size of the MRI image dataset and model complexity.	Yes

Table 36. Environmental Impact Ranking of Recycling

End of Life (Recycling/Management)				
ID	**Item**	**Environmental Impact Rank**	**Notes**	**Controllable?**
1	Software Maintenance	1	Regular updates for optimizing the algorithm could add to the energy costs required to run and maintain the processing pipeline.	Yes

15.2. Environmental Impact Comparison

This analysis compares the power consumption and environmental impact of three different approaches for MRI UTE to CT conversion:

1. Current Prototype without Machine Learning Integration
2. Deep Learning-Based Approach
3. Traditional CT Scan

1. Current Prototype (No Deep Learning)

The codecarbon python library was used to calculate the power consumption for the current preprocessing pipeline converting between UTE-MR and pCT when run locally [117].

Table 37. Environmental Impact Calculation of Current Prototype

Assumptions: Power consumption was calculated using basic CPU and RAM usage, not GPU utility. Eco-intensity impact is obtained from the average CO_2 emitted per kWh within Canada.				
Sources: Code Carbon [117] and Provincial and Territorial Energy Profiles [118]				
Eco-Intensity (impact/kWh)	**Power Consumption (kWh)**	**Uncertainty (%)**	**Calculated Impact**	**Ionizing Radiation**
0.1 kg CO2 per kWh	0.000212 kWh	10%	0.000021	NA

2. Deep Learning Based Approach (Multi-cycle GAN + UNet)

As the deep learning based portion of the workflow was unable to be fully implemented due to time constraints, the precise power consumption of this approach was not computed. Hence, exact numbers will only be derived after full-scale implementation in future refinements.

Table 38. Environmental Impact Calculation of Deep Learning Approach

Assumptions: Power consumption was calculated using a benchmark application for a 2-layer neural network implemented via TensorFlow, a popular machine learning library. The UNet or Multi-cycle GAN architecture is assumed to consume similar amounts of energy as a Convolutional Neural Network (CNN) model. Eco-intensity impact is obtained from the average quantity of CO_2 emitted per kWh within Canada.				
Sources: Neural Designer [119] and Provincial and Territorial Energy Profiles [118]				
Eco-Intensity (impact/kWh)	**Power Consumption (kWh)**	**Uncertainty (%)**	**Calculated Impact**	**Ionizing Radiation**
0.1 kg CO2 per kWh	4.5 kWh	100 %	0.45	NA

3. **Traditional CT scan**

Table 39. *Environmental Impact Calculation of Traditional CT Scan*

Assumptions: Energy and power consumption estimates were derived based on literature, and computed on average for each scan from a CT examination.				
Sources: Heye et al. [120], ScienceDirect [121], and FDA [122].				
Eco-Intensity (impact/kWh)	**Power Consumption (kWh)**	**Uncertainty (%)**	**Calculated Impact**	**Ionizing Radiation**
0.98 kg CO2 per kWh	1.2 kWh per scan/examination	10%	0.245	1-10 mSv per scan

16. Revised Specifications

Based on findings from the FTA and LCA exercises, our specifications, specifically the needs and requirements, were updated to maximize design robustness (*Table #40, 41*).

Table 40. *Revised Specifications - Needs*

Specification	Revised Specification	Justification
N/A - NEW	7.0: Input Validation and Error Messaging	User error was highlighted as a significant source of failure corresponding to when non-MRI images are added as input. Implementing automated image verification and preprocessing checks with clear error messaging would address this failure point.

N/A - NEW	8.0: Memory Management and System Stability	Memory leaks and excessive data sizes were outlined from the FTA as risks to system stability that can lead to processing failures or crashes. Optimized memory allocation techniques are recommended for pipeline reliability.
N/A - NEW	9.0: Algorithm Robustness	Algorithmic failures related to faulty bias correction, thresholding, and segmentation were also identified as potential failure points requiring fine-tuning of parameters and validation against diverse datasets for better generalizability.

Table 41. *Revised Specifications - Requirements*

Specification	**Revised Specification**	**Justification**
N/A - NEW	Requirement 7: ML Model Validation	Must implement k-fold cross-validation with diverse datasets to prevent overfitting.
N/A - NEW	Requirement 8: Input Validation	Must correctly identify and reject 100% of non-MRI images with appropriate error messages.

BMEG 457 – Design History File (DHF) 7.

April 11, 2025

Client: Siemens Healthcare Ltd. (Siemens Healthineers Canada)

Project: Magnetic Resonance Imaging (MRI)-Based Pseudo Computed Tomography (pCT) Generation Using Ultrashort Echo Time (UTE) Technique

Team #17: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen

Faculty Supervisor: Tim Salcudean

Report Type: Alpha Design

Word Count: 901

Abstract

The following document focuses on the creation of a preliminary model for the image processing software which captures the significant modules for conversion from UTE-MR to pseudo-CT. Moreover, the report outlines next steps to completion of the first-pass, alpha prototype and is accompanied by a presentation that demonstrates the modular design to an audience.

XIII. *Table of Contents*

19. Alpha Design Creation

In this section, we focused on developing our alpha design prototype that demonstrates the core functionalities of our MRI to pseudo-CT processing pipeline. We documented our development process through screenshots, diagrams, and test results that verify our system's ability to perform its intended functions, with a particular focus on critical requirements outlined in our specifications. Predominantly, this included accurate segmentation of soft-tissue and bone.

20. Completion Plan

Our Completion Plan outlines the remaining work needed to finalize our alpha design. We created a concise document detailing each step's status, team member responsibilities, timelines, and critical aspects that require particular attention for successful implementation.

28th February, 2025

Team: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen
Client: Siemens Healthcare Ltd. (Siemens Healthineers)
Faculty Supervisor: Tim Salcudean

The following document outlines the state of the alpha design and highlights steps to completion.

1. What steps are/will be taken?

The group dedicated the past few weeks iterating upon the two most significant modules of the image processing prototype: bias correction for rectification of inhomogeneities, and automatic thresholding for bone-soft tissue segmentation, with some progress on registration as well.

Based on our most recent meeting with Dr. Lumeng Cui, the team was advised to continue investigating the robustness of the pipeline by testing its performance on unseen UTE-MR datasets for the shoulder and knee provided by the client. In parallel, the group will be focusing on consolidating the different processing modules into a single, comprehensive executable file.

2. What is the status of each step?

Currently, the N4ITK package paired with hyperparameter optimization yielded the narrowest histogram peaks after performing inverse-logarithmic scaling for bias correction. Meanwhile, automatic thresholding combined with morphological closing for a relatively large kernel size showed marginal improvement over manual thresholding for segmentation of the background, cortical bone, and soft tissue masks. Finetuning of the parameters and experimentation with other packages such as SITK and skimage.morphology would be conducted to optimize the output.

3. Who is in charge of which aspects?

Yuheng Zhang and Manan Verma are responsible for the histogram-based bias correction. Meanwhile, Lynn Alvarez Krautzig is the assigned group member for the gaussian fitting and thresholding components. Jackson Chen and Aly Khan Nuruddin are responsible for integration of the workflow modules, with the latter also contributing to the administrative side of the project. All team members will participate in completing documentation and attending meetings.

4. When will it be done?

A tentative deadline for completion of the alpha-design has been set for Monday, March 3rd as the group will be presenting a mock run-in of the prototype to the client on Tuesday, March 4th.

5. What are the critical aspects of each task?

At this stage, the important considerations for the working prototype include evaluating each module's performance by testing with the provided data and up-scaling into a singular pipeline.

21. Client Review Plan

We prepared and sent a brief communication to our client summarizing our alpha design's purpose and progress to date. This section includes our original email memorandum.

Email Memorandum

Hello Dr. Cui,

Thank you for taking out your time to meet with our team and for sharing your insights on our image processing prototype. We sincerely appreciate all your support on the project so far.

The following paragraph will provide a brief summary of the work performed by the team to date while outlining subsequent steps for iterative design and consolidation into a working pipeline:

<u>Summary of Alpha-Design</u>
Our current prototype inputs Magnetic Resonance (MR) images acquired using an Ultrashort Echo-Time (UTE) sequence and outputs its corresponding pseudo-Computed Tomography (pCT) scans. First, the UTE-MR images undergo inverse-logarithmic scaling to enhance cortical bone contrast with intensity normalization for cross-modality comparison. Next, a histogram-based bias correction technique is applied to adjust signal inhomogeneities using the N4ITK module in tandem with manual hyperparameter optimization to yield the sharpest histogram peaks. Subsequently, an automatic thresholding method is implemented with morphological closing to speed up the downstream design process for image segmentation. However, prior to this module, Gaussian fitting is utilized to compute the upper and lower thresholds using the full-width half-maximum of the signal and noise peaks. Correspondingly, the generated segmented images retain contrast between cortical bone and soft-tissue while aptly removing background noise. The value proposition of the imaging pipeline is to provide supplementary diagnostic information to radiologists through an alternative modality like pCT while using existing MRI machines.

Attached kindly find a copy of our Meeting Minutes with documentation of the main talking points, expectations and deliverables for next week. Additionally, I have included our Progress Update Presentation which highlights our most up-to-date results for your kind perusal.

In this regard, our group would be eager to arrange for a meeting to review the design. This would provide us with the opportunity to formally present our comprehensive device and to obtain your constructive feedback on the technical robustness of our software product.

We would be very grateful if you could please let us know your availability for the month of March to schedule an hour-long meeting so we can showcase our design to you and your team.

Eagerly looking forward to hearing from you soon and thank you in advance.

Sincerely,
Aly Khan Nuruddin (Client Liaison - Team #17)

22. Alpha Design Presentation

Please click on the link below to access our Alpha Design Presentation Slides:

7.4. Alpha-Design Presentation

BMEG 457 – Design History File (DHF) 8.

April 11, 2025

Client: Siemens Healthcare Ltd. (Siemens Healthineers Canada)

Project: Magnetic Resonance Imaging (MRI)-Based Pseudo Computed Tomography (pCT) Generation Using Ultrashort Echo Time (UTE) Technique

Team #17: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen

Faculty Supervisor: Tim Salcudean

Report Type: Detailed Design

Word Count: 2208

Abstract

The following document describes the finalized design components of the digital image conversion tool for hand-off to the client. A summary of the complete specifications is included, along with the entire code repository with comments for ease of use. To fully capture the standard operating procedures, compiler requirements, and an instruction manual is also given.

XIV. *Table of Contents*

XV. *List of Tables & Figures*

23. Description of Finalized Design

This section presents our finalized MRI to pseudo-CT pipeline design, including detailed explanations of all subsystems, components, and processing workflows. Annotated visualizations are provided to showcase key features and operational sequences in the implementation context.

23.1. Design Overview

The finalized design is an image processing pipeline that effectively generates synthetic CT images from UTE-MR images. This workflow focuses on addressing the major challenges that are encountered while obtaining CT images such as intensity inhomogeneities, low bone contrast and poor bone-air separation. The generated synthetic CT images aim to provide enhanced anatomical details while preserving the soft-tissue contrast which is better resolved in MRI. Thereby, the strengths of MRI in soft-tissue visualization and the strengths of non-ionizing CT are combined to provide the best of both worlds within the field of diagnostic radiology.

This critical function prototype flowchart represents the complete sequence for generation of pseudo-CT output from UTE-MR input, providing a clear overview of the image processing steps that are undertaken in the pipeline (*Figure #17*) . Predominantly, these critical functions comprise of bias-field correction, inverse logarithmic scaling and thresholding.

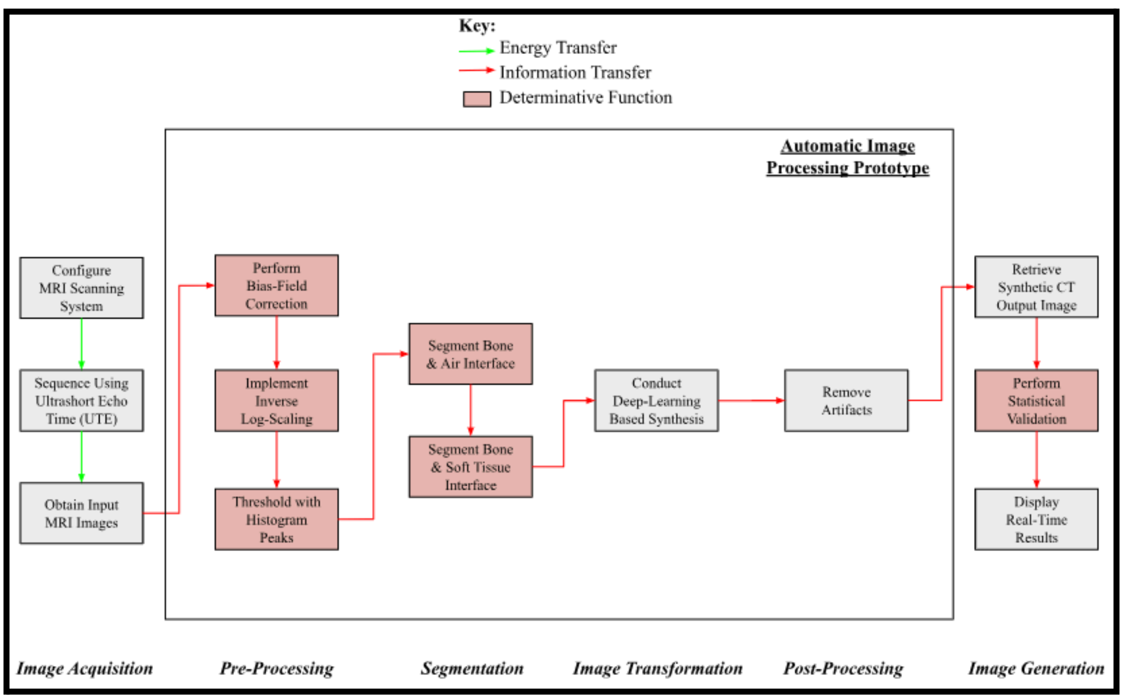


Figure 17. *Critical Function Prototype Flowchart.*

Additional operations such as Gaussian fitting and histogram analysis facilitated identification of the thresholds for image segmentation. The table below provides a summary of these components of the automatic image processing pipeline (*Table #42*).

Table 42. *Summary of Components of Image Processing Pipeline*

Step	Function	Components
Bias Correction	Corrects intensity inhomogeneities, improves soft-tissue contrast and reduces artifacts.	N4ITK with hyperparameter optimization, OpenCV,
Inverse Logarithmic Scaling	Significantly enhances the contrast of the bone signal.	Numpy used to apply log scaling and take inverse
Histogram Analysis	Identifies and visualizes the signal peaks.	Histogram calculation with Numpy
Gaussian Fitting	Fits Gaussian curves to the histogram for accurate thresholding.	Gaussian Mixture Model (GMM)
Automatic Thresholding	Automatically identifies threshold from the corresponding histogram.	Scipy (FWHM calculation)
Segmentation	Classifies pixel intensities into different regions such as bone, air and soft-tissue, based on the identified thresholds.	OpenCV (morphological operations)

Bias Correction

This is the first major processing operation on the input UTE-MR image that is required to correct for intensity variations prevalent due to the bias-field [123]. For our pipeline, this has been implemented using the N4ITK algorithm. This N4ITK bias correction method also has multiple hyperparameters which have been optimized systematically to generate the most optimal correction results and to derive the best histogram from the preceding inverse logarithmic scaled image. These hyperparameters are spline order, convergence threshold, number of histogram bins and number of iterations, which were fine-tuned iteratively.

Another bias correction method explored in our prototyping phase was a histogram-based approach, which utilizes intensity distributions of the image. From a comparative analysis of our results, this method did not generate significant improvements within the histogram and bias corrected image. Thereby, in our final pipeline, we decided not to include this approach, instead solely relying on the N4ITK module to optimize compute performance and workflow efficiency.

Inverse Logarithmic Scaling

This module is implemented on the input UTE-MR image following hyperparameter-optimized N4ITK bias correction to enhance the lower intensity variations, making them more distinct and distinguishable. Hence, this technique is crucial for obtaining improved bone visualization and facilitates adequate separation of the bone-air interface.

Histogram Analysis and Gaussian Fitting

A histogram of the inverse logarithmic scaled image is generated in order to analyze the distribution of pixel intensities and facilitate identification of the two major peaks, which correspond to the soft-tissue and background. Gaussian fitting is then applied to smoothen the histogram for more accurate intensity distributions and easier distinctions between the signal and noise centers. The pipeline uses a GMM (Gaussian Mixture Model) to perform this step.

Automatic Thresholding

The results of the Gaussian fitting are then utilized to automate the accurate identification and separation of the two major peaks from the histogram. Threshold selection was conducted using the formula for Full-Width Half Maximum (FWHM), specifying the lower and upper boundaries [124]. Thus, this method helps improve the consistency and accuracy of thresholding.

Segmentation

The final step within our pipeline involves utilizing the thresholds of pixel intensities to divide the synthetic-CT images into distinct anatomical regions, consisting of soft-tissue, bone and air, by generating masks. Morphological closing was applied to further refine the segmentation results, which aided in removing small holes and discontinuities from the resultant image through application of a kernel [125]. Lastly, distinct grayscale values are assigned to each region of bone, air and soft-tissue for visualization of the fully segmented pseudo-CT images.

23.2. Assumptions & Limitations

Assumptions

The following assumptions were undertaken to help define the scope of the pipeline while ensuring the generation of consistent and accurate pseudo-CT outputs from UTE MRI images:

1. Images are acquired using standardized MRI scan protocols with constant Echo Time (TE) and Repetition Time (TR). This ensures uniform tissue contrast, leading to reliable downstream p-CT generation while reducing variability due to acquisition differences.
2. Images are extracted using an Ultrashort Echo Technique (UTE) sequence from short-T2 tissues, with a strong bone signal that is well-represented in the acquired MR image.
3. Outliers like noise, artifacts, or unusual anatomy do not significantly impact statistical pre-processing steps such as bias correction and normalization, indicating robustness.
4. The pipeline is MRI scanner-agnostic, supporting clinical scalability, cross-site deployment and scalability while tolerating variations in hardware specifications.
5. Images are considered free of motion-induced distortions, which could otherwise blur tissue boundaries and reduce the accuracy of pseudo-CT generation.

Limitations

The pipeline also has certain limitations which can impact its performance and generalizability over larger datasets or images with more complex anatomical characteristics. These are specified below:

1. The pipeline is currently developed and evaluated on a small dataset, which may limit its ability to capture anatomical and pathological variability.
2. There has been limited testing across different body regions or subject types (e.g., pediatric vs. adult, healthy vs. pathological), which constrains the pipeline's applicability.
3. The workflow does not yet incorporate machine learning models, relying instead on traditional processing methods, thus limiting potential performance improvements.

24. Final Specifications

This section provides comprehensive technical documentation sufficient for another group of engineers to reproduce our system. Thoroughly commented code for our image processing algorithms, detailed specifications of required computing resources, and complete parameter settings for each processing module have been provided for a holistic reference.

24.1. Summary of Specifications

Device Overview

This device is a software-based medical tool that generates pseudo-CT (pCT) images from MRI scans with Ultrashort Echo Time (UTE) sequences. The system processes MRI data through a series of image processing steps to create CT-like images without requiring patients to undergo CT scans, thus saving operational resources while providing high-quality diagnostics.

Regulatory Classification

The software prototype is classified as a Class II Software as a Medical Device (SaMD) under Health Canada regulations [126, 127], requiring a Medical Device License (MDL) before distribution [128]. The processing workflow must comply with ISO 13485 standards and adhere to the Canadian Personal Information Protection and Electronic Documents Act (PIPEDA) to safeguard patient privacy through use of anonymized datasets [129, 130, 131].

Functional Requirements

Geometric Fidelity Ensures accurate spatial representation of anatomical structures. The *Average Symmetric Surface Distance (ASSD)* between the generated pCT and reference CT images must be less than 1mm [132, 133].
Bone-Air Interface Segmentation Quantifies the system's ability to differentiate between air and bone in the generated images. Must achieve an *Area under the ROC Curve (AUC)* value of at least 0.976 [134].
Image Quality Must achieve a *Peak Signal-to-Noise Ratio (PSNR)* of at least 20 dB [135]. Must obtain a *Structure Similarity Index Measurement (SSIM)* value of at least 0.6 [136, 137]. Must achieve a *Dice Similarity Coefficient (DICE)* of at least 0.83 [138, 139].
Intensity Distribution Accuracy Must achieve *Mean Absolute Error (MAE)* values of less than 174 for bone, less than 22 for air, and less than 159 for soft tissue [140].

Technical Implementation

The following image processing steps are required to generate pCT from UTE-MR:

1. Data Input: Load grayscale UTE MRI images.
2. Bias Field Correction:
    - Implemented using the N4ITK module.
    - Optimized parameters:
        - Spline Order: 2
        - Convergence Threshold: 10^{-3}
        - Number of Histogram Bins: 50
        - Maximum Number of Iterations: [50, 50, 50, 50]

3. Image Normalization:
    - Normalize corrected image to [0-1] range.
    - Apply inverse log scaling: `log_image = np.log(corrected_image + 1)`
    - Convert to 8-bit format: `log_image = np.uint8(255 * log_image)`
    - Invert image: `inverse_log_image = 255 - log_image`
4. Automatic Thresholding:
    - Implement Gaussian Mixture Model (GMM) with 3 components.
    - Extract signal and noise centers with standard deviations.
    - Calculate Full Width at Half Maximum (FWHM):

```
signal_fwhm = 2*np.sqrt(2*np.log(2))*sorted_std_devs[0]
noise_fwhm = 2*np.sqrt(2*np.log(2))*sorted_std_devs[2]
```

    - Set lower and upper thresholds:

```
lower_threshold = signal_center + 2*signal_fwhm
upper_threshold = noise_center - 2*noise_fwhm
```

5. Segmentation:
    - Create masks for different tissue types:
        - Soft-tissue: `inv_norm < lower_threshold`
        - Bone: `(inv_norm >= lower_threshold) & (inv_norm < upper_threshold)`
        - Air: `inv_norm >= upper_threshold`
    - Apply morphological closing with elliptical kernel (7,7).
    - Assign grayscale values to segments:
        - Air: 0 (black)
        - Soft-tissue: 128 (mid-gray)
        - Bone: 255 (white)
6. Registration:
    - Non-rigid registration using B-Spline transform.
    - Implementation through SimpleITK library.

Dependencies

- Python libraries required:
    - OpenCV (cv2)
    - NumPy
    - SimpleITK
    - Matplotlib
    - SciPy
    - scikit-learn (for GMM)
    - nibabel (for NIFTI file handling)

Future Improvements

1. Leveraging publicly available datasets for training and validation of deep learning models, thus enabling more robust and scalable pseudo-CT synthesis.
2. Adapting the pipeline to support the NIFTI (.nii/.nii.gz) format, which is widely used in medical imaging, for volume-based computation and improved interoperability.

24.2. Full Code with Comments

Click the link below to view the full commented code for the entire workflow:
8.2-2 Full Code w/ Comments.pdf

24.3. Computer Specifications

To run the code smoothly, the following specifications are recommended:

Processor & Hardware

- Operating System: Windows 10 or later
- Processor: Any modern x86-64 processor (e.g., Intel Core i5/i7 or AMD Ryzen) should be sufficient.
  - A GPU is not necessary but can accelerate image processing tasks.
- RAM: At least 8 GB is recommended, though 16 GB or more may improve performance when processing larger image files.

Software

- Python Version: Python 3.8 or higher
- These Python libraries are required:
  - numpy
  - cv2 (OpenCV)
  - SimpleITK
  - matplotlib
  - scipy
- Jupyter Notebook: Recommended for running the .ipynb file directly.

25. Instructions for Use

We developed a clear and concise standard operating procedure for our processing pipeline, which provides step-by-step instructions for users with varying technical backgrounds.

Introduction

This guide provides clear instructions for setting up, operating, and troubleshooting the image processing workflow to convert Ultrashort Echo Time (UTE) MRI to pseudo-CT scans.

Installation Instructions

System Requirements:

- Operating System: Windows 10 or later
- Python 3.8 or later
- Recommended IDE for easier code navigation and debugging:
  - Visual Studio Code (VS Code) or PyCharm
- Required Libraries: numpy, cv2, SimpleITK, nibabel, matplotlib, scipy, scikit-learn

Installation Steps:

1. Install Python from python.org
2. Install VS Code from code.visualstudio.com or PyCharm from jetbrains.com
3. Install the Python and Jupyter extensions for VS Code to run the `.ipynb` files.
4. Install required libraries by running the following command in your terminal:

```
pip install numpy opencv-python SimpleITK nibabel matplotlib scipy scikit-learn
```

- Ensure your working directory is correctly set to the folder containing the project files.

Operating Procedure

Step 1: Running the Code in Jupyter Notebook

Launch Jupyter Notebook by running the following command in your terminal:

```
jupyter notebook
```

- Open the `.ipynb` file in the Jupyter interface.
- Follow the code sequentially, executing each cell by pressing `Shift + Enter.`

Step 2: Image Loading

- Place the desired image file (e.g., image.png) in the working directory.
- Update the `image_path` variable in the code to match your file name.

Step 3: Bias Field Correction

- The code uses the N4ITK algorithm to correct intensity non-uniformities.
- Key adjustable parameters include:
  - Spline Order: Recommended value is **2**
  - Convergence Threshold: Recommended value is $\mathbf{10^{-3}}$
  - Number of Histogram Bins: Recommended value is **50**
  - Maximum Number of Iterations: Recommended value is **50**

Step 4: Inverse Log Scaling

- The corrected image is normalized and log-transformed to improve contrast.
- The result is saved as CFP_inverse_log_scaled_image_presentation.png
  - Feel free to adjust this name as you feel necessary.

Step 5: Histogram Analysis and Thresholding

- The code identifies peaks corresponding to noise and signal levels using a histogram.
- The Gaussian Mixture Model (GMM) fits the data for better threshold precision.

Step 6: Image Segmentation

- The code applies thresholds to classify pixels as:
  - Soft-Tissue
  - Bone
  - Air
- Results are saved as Closed_CFP_segmented_image_automatic_presentation.png
  - Again, adjust the file name as you feel necessary.

Safety and Precautions

- Ensure all medical images are de-identified to comply with data privacy regulations.
- Avoid overwriting important image files by renaming outputs appropriately.
- When adjusting Gaussian Mixture Model parameters, test on sample data to avoid adding excessive noise to the system.

Troubleshooting

Error: Image File Not Found

- Verify that the file path in image_path is correct.
- Double check that the image file is saved in the correct directory.

Error: Incorrect Image Output

- Check the histogram plot to confirm threshold values are properly identified.
- Adjust the GMM parameters to improve segmentation accuracy.

Error: Missing Libraries

- Run pip list in your terminal to confirm required libraries are installed.
- If missing, reinstall libraries using pip install <library_name>

Maintenance and Updates

Periodically update dependencies with pip install --upgrade <library_name>

- Regularly test the code with sample data to ensure continued accuracy.
- If hardware limitations impact performance, consider optimizing array operations for faster computation.

BMEG 457 – Design History File (DHF) 9.

April 11, 2025

Client: Siemens Healthcare Ltd. (Siemens Healthineers Canada)

Project: Magnetic Resonance Imaging (MRI)-Based Pseudo Computed Tomography (pCT) Generation Using Ultrashort Echo Time (UTE) Technique

Team #17: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen

Faculty Supervisor: Tim Salcudean

Report Type: Verification & Validation

Word Count: 3146

Abstract

The following document describes the tests undertaken by the group to rigorously assess whether the device suitably meets the expectations and specifications outlined in accordance with our primary stakeholder, Dr. Lumeng Cui. A detailed description of validation and verification plans is followed by a summary of the finalized software design for the eventual perusal of the client.

XVII. *Table of Contents*

XVIII. *List of Tables & Figures*

27. Supervisor Approval of Protocols

Supervisor Approval of Protocols
20th March, 2025

Team: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, Jackson Chen
Client: Siemens Healthcare Ltd. (Siemens Healthineers)
Faculty Supervisor: Tim Salcudean

The following document outlines the plan for verification of the various device modules:

- Registration of UTE-MR images will be performed with the corresponding pseudo-CT (pCT) and ground truth CT scans to achieve a one-to-one reference mapping. However, prior to this, the MR volume will be downsampled in 3DSlicer to facilitate comparison between corresponding slices. Rigid techniques will then be applied to correct for global shifts and rotations, while maintaining anatomical heterogeneity across pairwise pixels.
- Key features such as soft-tissue and cortical bone will be manually annotated to highlight the strength of the segmentation process for UTE-MR, pCT, and reference CT images. This labelling will allow for a simple, yet effective manner for visual identification of the different anatomical components within the complementary cross-modality images.
- Subtracting the UTE-MR from the pCT and true CT images will provide an alternative method to localize regions of deviation and identify structural inconsistencies. These absolute difference maps will be computed after converting all input volumes to a consistent numerical data type such as float or double, in order to avoid rounding or overflow errors. This approach also provides an intuitive way to observe the spatial distribution of errors and can inform improvements to the pCT generation pipeline.
- The histogram of both pCT and reference CT will be computed to assess intensity distribution across the tissue types. Following Wiesinger et al. (2015), Gaussian fitting will first be applied to identify peaks for soft tissue and noise, with bone intensities distributed in between. Thresholds derived from peak centers and FWHM values will enable automated segmentation and analysis of signal distribution over tissue classes.
- Lastly, a suite of quantitative metrics will be used to evaluate the fidelity of pCT images obtained from our prototype. Structural Similarity Index (SSIM) will assess how perceptually similar the pCT is to the true CT, accounting for spatial content. Meanwhile, the Dice Similarity Coefficient (DICE) will be calculated based on overlap between segmented structures in the pCT and true CT. Finally, the Mean Absolute Error (MAE) will provide a direct, voxel-wise quantification of intensity deviation across the images.

To incorporate usability and clinical relevance into the validation process, user evaluation will be obtained from the client, Dr. Lumeng Cui, based on the NASA Task Load Index (TLX) scale. This will permit the MR Collaboration Scientist to assess the prototype based on perceived workload dimensions such as mental demand, effort, frustration, and timeliness. Hence, the given feedback will allow for fine tuning of design parameters to ensure real-world applicability.

28. Validation - User Evaluation

28.1. Motivation

This user evaluation plan is designed to ensure that the image processing prototype is easily integrated into the existing workflow of a radiologist and performs as intended. As our team does not have experience with analysis of medical images, incorporation of a user who is familiar with the key features that define a successful pseudo-CT conversion is invaluable. Ultimately, the feedback obtained from this user evaluation plan will identify further areas of refinement, especially with regards to the intuitiveness of the design for clinical implementation.

28.2. Introduction

The image processing workflow is designed to intake UTE-MR images uploaded by the user. Correspondingly, the prototype will process the image following the steps previously outlined in DHF-8 to generate the corresponding, well-segmented pseudo-CT image.

28.3. Methods

1. *Users:* For our validation process we will be recruiting our client, Dr. Lumeng Cui, an MR Collaboration Scientist from Siemens Healthineers, to evaluate our design. Throughout this project, we have been engaging in bi-weekly meetings with our primary stakeholder to gain feedback on our design. Although the end-users of this prototype will be radiologists, it was beyond the scope of the project for the group to establish timely contact with such individuals. However, as a clinical researcher, our client has sufficient pedigree and expertise within the field of medical imaging to adequately assess our prototype and guide future work for successive iterations of the digital product.

2. *Protocol:* The user will first be given access to our GitHub repository, which includes the code for our automated workflow. Our client will download the .png UTE-MR files provided in the documentation and update the input image path to match the location in the working directory. The user will then run the code and the UTE image will be converted to pseudo-CT. The process of this protocol is quite similar to a real use case where the software would convert a selected UTE-MR volume to synthetic-CT. However, one of the major differences between the prototype and a clinical-ready product is that our design only functions for select slices without scalability across the entire volume. As the protocol is intended to be simulated on a standard computer with limited compute performance, implementing volume-based differentiation was challenging due to time

and energy constraints, and therefore avoided. The final use case of this workflow would thus be integration with an MRI machine which possesses high processing capacity.

3. *Evaluation:* To evaluate our user-evaluation results, we will be providing the client with a survey to partake in after sufficient usage of the workflow. In particular, the document will utilize the NASA Task Load Index (TLX) to assess the workload over 5 seven-point scales (*Appendix 9-A*). The NASA-TLX Index is commonly incorporated for assessments in high-risk environments, such as the healthcare sector, where an increase in strenuous workload can have negative implications on diagnostics outcomes. Hence, it is critically important that the design is easily reproducible in medical settings for smooth conversion of UTE-MR into synthetic-CT while minimizing stress on radiologists and patients alike.

28.4. Results

The results from our user, Dr. Lumeng Cui, are presented below in the form of a survey, as captured by the NASA-TLX Index. These outcomes suggest that the client found it extremely straightforward to implement the prototype, without requiring significant effort. This was accompanied by minimal physical, mental, and temporal strain, as well as frustration. Additionally, the user also indicated that the prototype was successful in achieving an MR to pseudo-CT conversion. Initial interpretations of these results indicate that the user is happy with the task's workload. This position validation help reassure that the workflow could be easily integrated into clinical settings for radiologic interventions without a drastic increase in user stress.

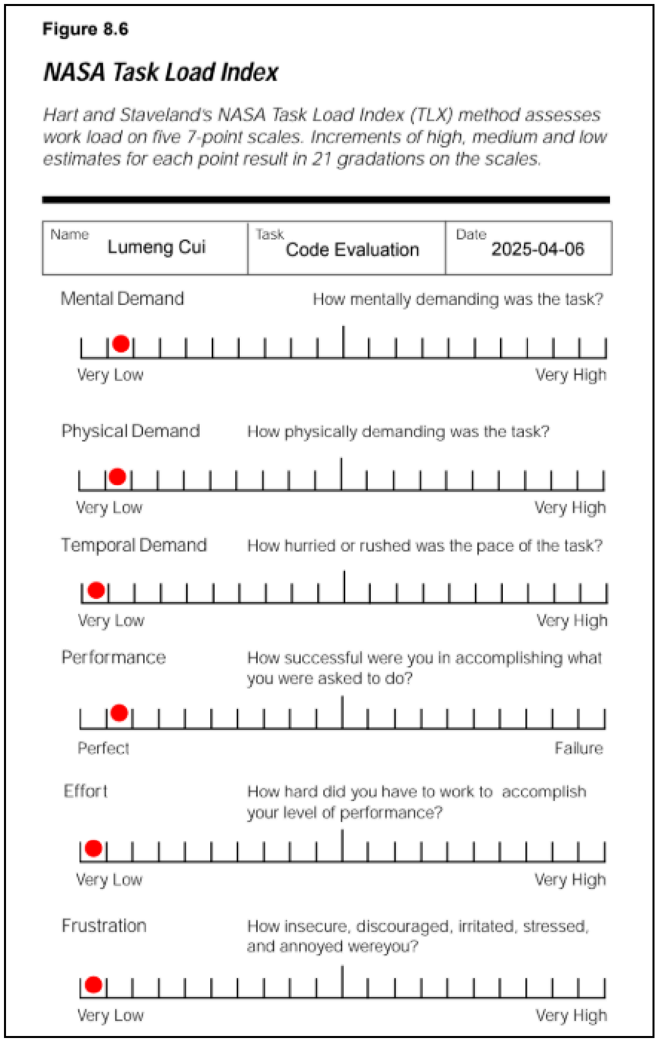


Figure 18. *User Response to NASA Task Load Index Survey*

28.5. Conclusion

From the results of the NASA Task Load Index evaluated by our client, Dr. Lumeng Cui, it is evident that the workflow is adequate for timely processing of images. These outcomes validate *Need #7 - Timeliness of Procedure*, previously outlined in DHF #1, which highlights that the prototype should reduce the time needed to convert the UTE MRI to a pseudo-CT.

While the results obtained are favorable and indicate minimal need for improvements, it is important to contextualize the NASA-TLX feedback when considering potential updates to the workflow. The low time demand reported may be attributed to the use of individual MRI slices rather than full volumes, which reduced processing and interaction time. Additionally, the user, Dr. Lumeng Cui, has a strong technical background, which may have influenced their perception of the overall workload. As such, for a more comprehensive and generalizable evaluation, future testing should include end-users such as radiologists, who may not necessarily have the same expertise with medical software. Moreover, collecting feedback from a larger and more diverse user base will be essential to validate the workflow's usability and adaptability in real-world clinical settings. This is critical to holistically appraise the performance of the imaging prototype.

29. Verification - Evaluation of Specification

29.1. Dice Similarity Coefficient (DSC)

<u>*Aims:*</u>

The goal of evaluating the DICE Similarity Coefficient (DSC) is to quantify the overlap between the segmented regions of the true CT and the pseudo-CT for bone, soft-tissue, and air.

<u>*Methods:*</u>

The ground truth CT and UTE-MR images were first manually registered using 3DSlicer to downsample and align the cross-modality scans. After registration, a single slice from both the CT and MR was saved as a .png file. The specific slice of the MR used for registering the CT was then used as the input for the workflow. After obtaining the resulting pseudo-CT, the previously registered CT and pseudo-CT were used to calculate the DSC. The DSC was computed in Python using the formula below (*Equation 2.*), where 'A' represents the ground truth CT, and 'B' represents the pseudo-CT. DSC scores will range between 0 and 1, with 0 indicating no similarity between the images and 1 showing that the images have perfect overlap.

$$\frac{2|A \cap B|}{|A|+|B|}$$

Equation 2: *DSC Calculation*

Referring to the updated specification outlined in *DHF #2*, the design was required to obtain a DSC score of 0.83. The evaluation curve for this metric is presented below, with values greater than 0.83 increasing client satisfaction linearly, reaching 100% at a DSC score of 0.94 (*Figure 19*). Hence, a DSC score of at least 0.83 would be needed for this evaluation criterion.

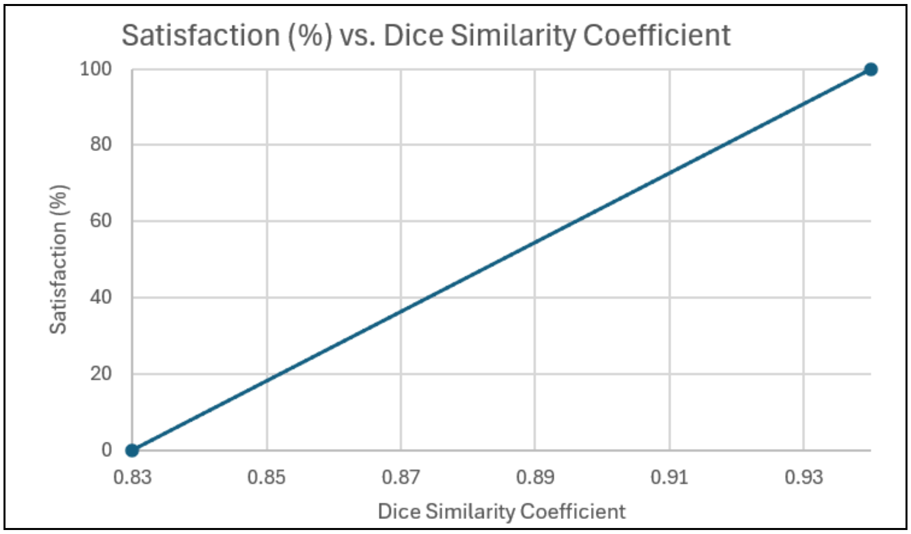


Figure 19. *Evaluation Curve for DSC.*

<u>Results:</u>

A DSC score of **0.7986** was obtained using the paired pseudo-CT and reference CT. The images below show the input UTE MR, generated pseudo-CT and the reference CT slices used for finding the DSC (*Figure 20*). This fails the outlined specification of 0.83.

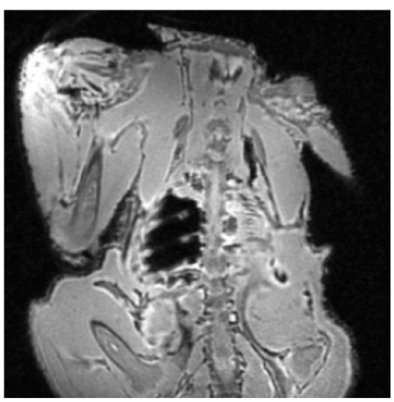
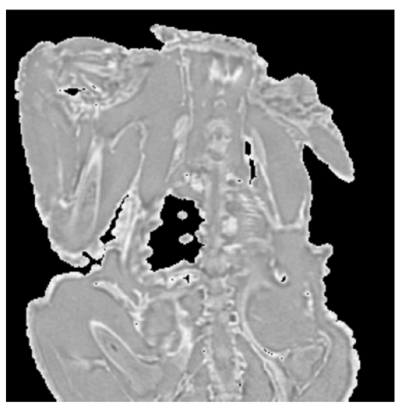
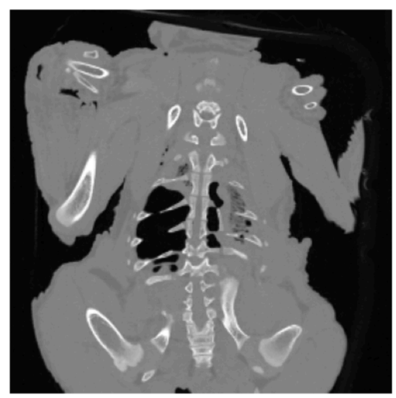
		
UTE MRI	Pseudo-CT	CT

Figure 20. *Paired UTE MR Slice, Generated Pseudo-CT and Reference CT of Chicken Dataset.*

<u>Discussion:</u>

From the results, we observe that the specification has failed by a small margin. To further investigate this metric, it would be important to repeat the DSC scoring with other paired CT-MR slices to ensure that the nominally lower value is not due to poor registration between images. However, the DSC score was quite close to the requirement which helps verify that the workflow is moving in the right direction. Going forward, additional methods could be looked at to improve this value. One particular area that could ameliorate results would be to improve the outer edges of the pseudo-CT, which have a thick white border outlining the chicken's body.

29.2. Structure Similarity Index Measurement (SSIM)

Aims:

The aim of evaluating this metric is to quantify the structural similarity between the pseudo-CT and the true CT. This allows for assessment of how accurately the pseudo CT preserves anatomical structures, especially for cortical bone, when compared to the true CT.

Methods:

To calculate the SSIM score between pseudo-CT and true CT, image registration was first performed to ensure that both the MRI and CT volumes for the chicken dataset were accurately mapped. Following registration, a slice pair of the pseudo-CT and the true CT were used to calculate the SSIM score in Python using the skimage.metrics library from sci-kit-learn [141].

The following graph outlines the satisfaction curve for SSIM metric (*Figure 21*). A minimum score of 0.60 would need to be obtained to satisfactorily pass this evaluation criterion.

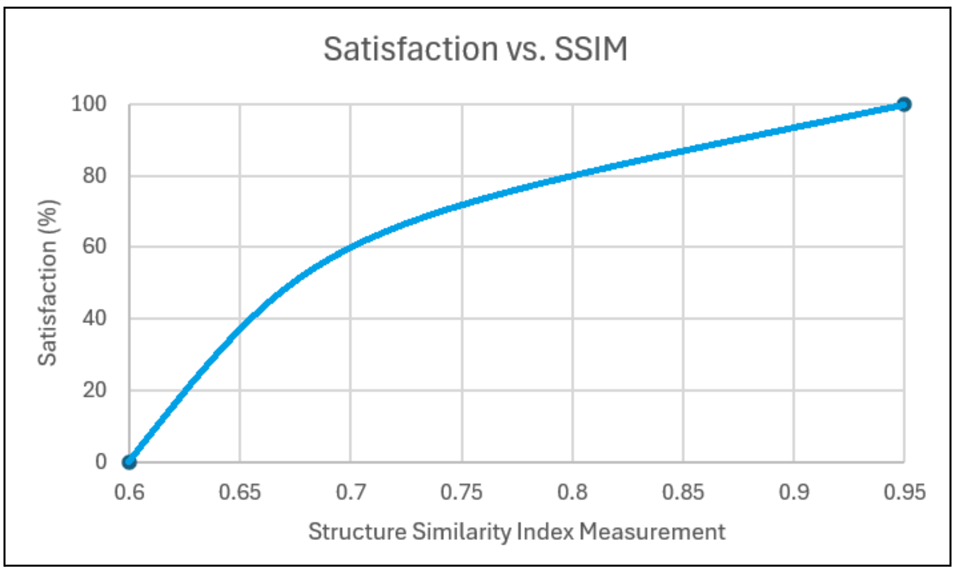
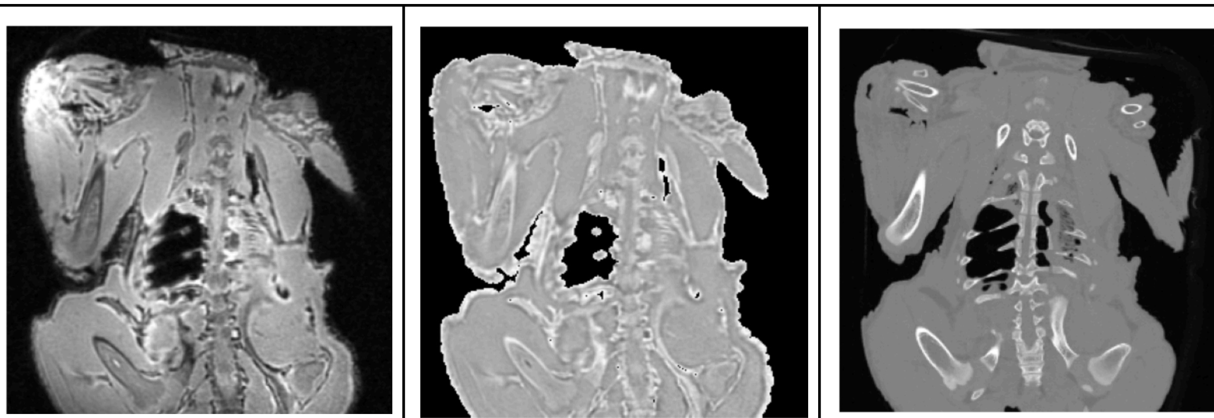


Figure 21. *Evaluation Curve for Structure Similarity Index.*

Results:

A SSIM score of **0.1976** was obtained using the sets of images below (*Figure 22*). This metric quantifies visual similarity between pseudo-CT generated from UTE-MR and the true CT. Since our value is way below the expected threshold, the prototype fails this specification.



UTE MRI	Pseudo-CT	CT

Figure 22. *Paired UTE MR Slice, Generated Pseudo-CT and Reference CT of Chicken Dataset.*

<u>Discussion:</u>

A low Structural Similarity Index Measurement (SSIM) with a high Dice Similarity Coefficient (DSC) typically indicates that while the structural shapes are well-aligned, as reflected by the DSC, the intensity distributions differ significantly, resulting in a lower SSIM. Since an SSIM score of 1 represents perfect similarity, the score of 0.1976 achieved by our workflow suggests notable discrepancies in visual similarity. One major contributing factor is the slight misalignment introduced during manual registration of the UTE-MR and CT volumes, which was necessary due to substantial differences in their original orientations. These small registration mismatches can negatively impact SSIM calculations. Additionally, variations in brightness and contrast between the two modalities further contribute to the reduced SSIM score.

29.3. Peak Signal-to-Noise Ratio

<u>Aims:</u>

This metric measures the quality of the pseudo-CT compared to the ground truth CT image. While a majority of the PSNR is attributed to the MR acquisition process, techniques such as bias correction, implemented in our workflow, can help generate higher values.

<u>Methods:</u>

Similar to previous methods, the pseudo-CT and ground truth CT were first manually registered with one another and a resulting single slice was saved as a .png file. PSNR is calculated using the Mean Squared Error (MSE) between the pseudo-CT and reference CT (*Equation 3*). The PSNR was computed using the skimage.metrics library from sci-kit-learn [142].

$$PSNR = 20log_{10}\left(\frac{MAX}{\sqrt{MSE}}\right)$$

Equation 3*: PSNR Calculation*

As outlined in *DHF #1*, the specifications for the prototype required achieving a Peak Signal-to-Noise Ratio (PSNR) of at least 20 dB, as values below this threshold are generally considered insufficient for producing a clinically viable pseudo-CT. Literature reviewed previously indicates that typical PSNR values for pseudo-CT generation tend to fall within the mid-20 dB range. Therefore, attaining or exceeding this benchmark is critical to improving the quality of the output and aligning with client expectations for image fidelity and clinical utility. The following graph outlines the satisfaction curve for the PSNR metric (*Figure 23*). A minimum score of 20 would need to be obtained to satisfactorily pass this evaluation criterion.

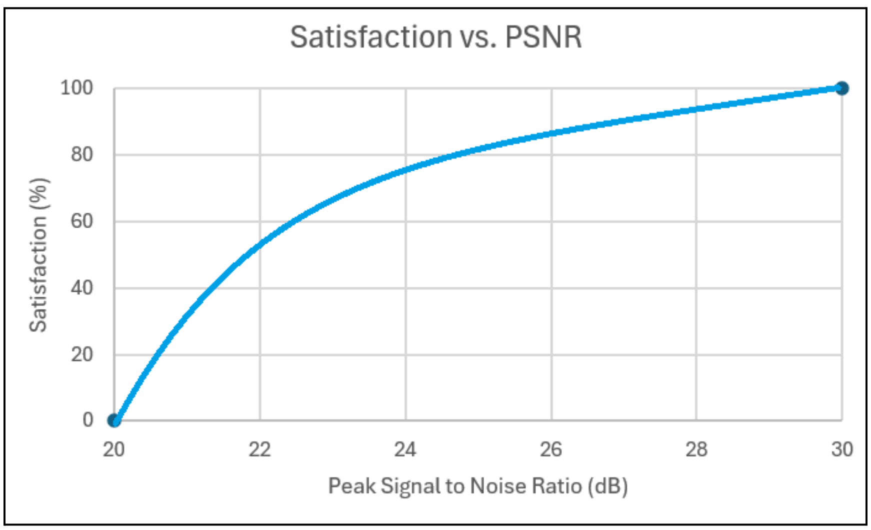


Figure 23. *Evaluation Curve for Peak Signal-to-Noise Ratio.*

<u>*Results:*</u>

A PSNR value of **15.48 dB** was obtained using the method described above, failing this specification. The table below shows the input UTE MR, generated pseudo-CT, and reference CT slices that yielded the best scores for this evaluation criterion (*Figure 24*).

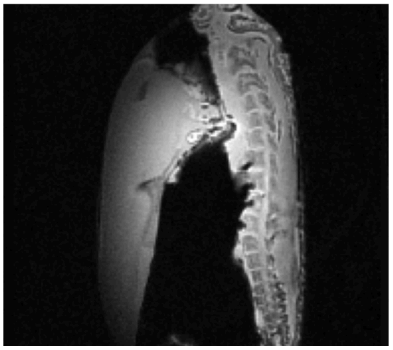
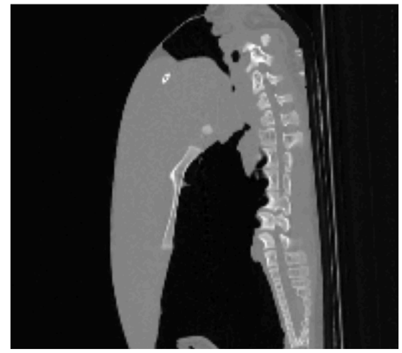
		
UTE MRI	Pseudo-CT	CT

Figure 24. *Paired UTE MR Slice, Generated Pseudo-CT and Reference CT of Chicken*

<u>*Discussion:*</u>

Qualitative assessment of the pseudo-CT reveals that the edges of the anatomical structure are not sharply delineated and appear slightly jagged compared to the reference CT, indicating limitations in structural fidelity. As previously discussed, one potential contributing factor to the lower-than-expected image quality scores may be registration inaccuracies between the pseudo-CT and MR images. To rule out registration as a primary source of error, it is recommended that the evaluation be repeated using an alternative dataset with pre-aligned CT-MR image pairs. This would enhance the robustness of our results for verification.

29.4. Conclusion

Based on the results from the specification tests, the generated pseudo-CT images exhibit issues in accurately outlining the contours of the chicken's body, with edges appearing jagged or surrounded by an unnatural white border. These visual artifacts likely contribute to the suboptimal performance observed in the validation metrics, specifically for the SSIM (*Table #X*).

Areas of refinement for the pseudo-CT workflow include improving image registration accuracy to minimize misalignment between MR and CT scans. Enhancing edge delineation is also necessary, as jagged or overly thick borders reduce visual fidelity. Addressing brightness and contrast mismatches between input and output images will improve structural similarity. Finally, testing the workflow on additional, well-aligned datasets will help determine whether current performance issues stem from the data itself or the algorithm's limitations.

Table 43: *Validation Plan Results*

Test #	Specifications	Testable Statement	Method	Pass/Fail Criteria	Result	Conclusion
1.	Evaluation	The	Use Python	A DSC	A DSC	FAIL

	Criteria #6	pseudo-CT and ground truth CT must indicate sufficient structural overlap.	to calculate the DSC score, comparing ground truth CT to pseudo-CT.	value of at least **0.83**.	score of **0.7968** was achieved.	
2.	Evaluation Criteria #4	The pseudo-CT and reference CT must have acceptable perceptual and structural similarity.	Use the scikit-learn library to calculate the SSIM score between the ground truth CT and pseudo-CT.	A SSIM score of at least **0.6**.	A SSIM score of **0.1976** was achieved.	FAIL
3.	Evaluation Criteria #2	The pseudo-CT output must ensure adequate intensity, fidelity and image quality.	Use Python to calculate the PSNR between the ground truth CT and pseudo-CT.	A PSNR of at least **20** dB.	A PSNR score of **15.48** dB was achieved.	FAIL

30. Updated Final Design

Following the execution of our validation plan, the workflow did not meet the predefined thresholds for DSC, SSIM, and PSNR. To address these shortcomings, we explored potential enhancements to the existing pipeline. Specifically, we investigated the impact of applying Contrast-Limited Adaptive Histogram Equalization (CLAHE), to enhance local contrast and structural visibility. CLAHE was applied post-segmentation using the given snippet (*Figure 25*)

```
clahe = cv2.createCLAHE(clipLimit=2.0, tileGridSize=(8, 8))
segmented_image = clahe.apply(segmented_image)
```

Figure 25. *Python Code Snippet Added to Improved Workflow*

The illustration showcases the MR slice used to generate the pseudo-CT with the updated workflow, alongside a comparison to the pseudo-CT produced using the previous procedure.

Upon comparison, the pseudo-CT generated with the CLAHE-enhanced process, exhibiting an improvement in contrast, highlighting enhanced detail and contributing to overall image quality.

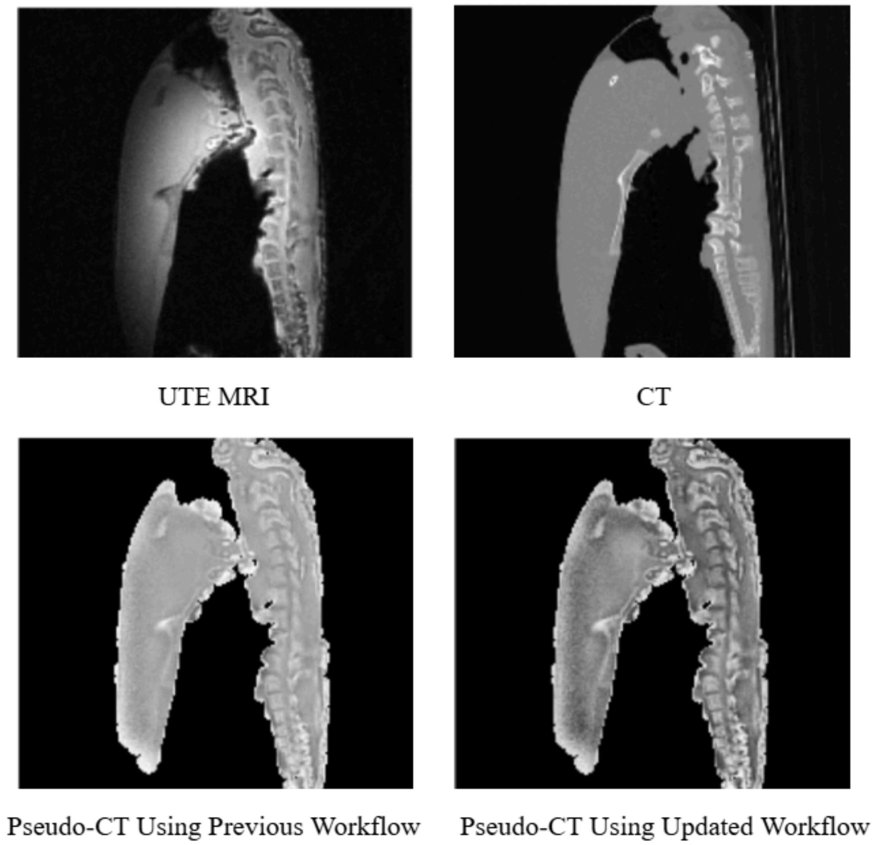


Figure 26. *Paired UTE MR Slice, Generated Pseudo-CT and Reference CT of Chicken Dataset.*

Using the same validation plan, we were able to obtain the following results which are summarized below for the updated workflow with CLAHE contrast enhancement (*Table 44*).

Table 44: *Validation Plan Results Using Updated Workflow*

Test #	Specifications	Testable Statement	Method	Pass/Fail Criteria	Result	Conclusion
1	Evaluation Criteria #6	The pseudo-CT and ground truth CT must indicate sufficient structural overlap.	Use Python to calculate the DSC score, comparing ground truth CT to pseudo-CT.	A DSC value of at least **0.83**.	A DSC score of **0.9994** was achieved.	PASS

2	Evaluation Criteria #4	The pseudo-CT and reference CT must have acceptable perceptual and structural similarity.	Use the scikit-learn library to calculate the SSIM score between the ground truth CT and pseudo-CT.	A SSIM score of at least **0.6**.	A SSIM score of **0.3500** was achieved.	FAIL
3	Evaluation Criteria #2	The pseudo-CT output must ensure adequate intensity, fidelity and image quality.	Use Python to calculate the PSNR between the ground truth CT and pseudo-CT.	A PSNR of at least **20** dB.	A PSNR score of **15.03** dB was achieved.	FAIL

The integration of CLAHE into the updated workflow led to noticeable improvements in both the DSC and SSIM scores, ultimately allowing us to meet our outlined specifications. This enhancement is particularly valuable as it aligns the results more closely with our validation requirements. While the PSNR showed a slight decrease after applying CLAHE, the change was minimal, and the score remained comparable to the previous results. Given the improvements observed in contrast enhancement and structural definition, we have determined that CLAHE will be a key component of our final design moving forward. This adjustment marks a significant step in refining the workflow and ensuring better quality in the generated pseudo-CT images.

M2.2. Design & Innovation Day Deliverables

M2.2.1. Abstract

Our project involves designing an automated workflow for generation of synthetic Computerized Tomography (sCT) scans from Magnetic Resonance (MR) images. While MRI is excellent for capturing details of soft-tissue, it struggles to accurately distinguish cortical bone from air. This lack of bone contrast has been a significant obstacle for using MRI in radiation therapy, despite its reliability in tumor diagnosis. As a result, CT remains the standard imaging protocol that radiologists rely upon for pre-operative planning.

However, a specialized MRI sequence called Ultrashort Echo Time (UTE) facilitates the detection of strong bone signals, allowing for the synthesis of CT-like scans through image processing. Hence, by converting MR into pseudo-CT images, our software product offers a radiation-free alternative to traditional CT scans for high-resolution visualization of the bone. This is particularly applicable for identification of complex fractures, eroded joints, and cancerous lesions.

Our workflow utilizes state-of-the-art techniques for correction of signal inconsistencies, enhancement of bone contrast, and segmentation of background noise. The prototype consolidates these image processing methods into a single executable file for seamless integration into clinical settings. The modularity of our design also allows for implementation of AI methods to enhance diagnostic quality.

Thus, our project aims to provide a practical solution for integration of MRI-based bone imaging in radiation therapy, leading to improved patient outcomes while reducing the reliance on standard CT scans.

M2.2.2. Poster

Please click on the link to view our Design and Innovation Day Poster:

Poster.pdf

M2.3. Client Interactions

M2.3.1. Emails

UBC-SBME Capstone

To: lumeng.cui@siemens-healthineers.com; alykhan5@student.ubc.ca

Cc: tims@ece.ubc.ca

Reply | Reply all | Forward

Wed 9/18/2024 14:37

Project 25 - Magnetic Reson...
157 KB

Hi Lumeng,

I am excited to introduce you to the 4th year Biomedical Engineering Capstone team that will be undertaking your project – Magnetic Resonance Imaging-based Pseudo Computed Tomography Generation Using Ultrashort Echo Time Techniques (I am attaching the project summary for reference). The team is Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, and Jackson Chen. Aly Khan Nuruddin (alykhan5@student.ubc.ca, CC'ed) will be responsible for communicating with you via email going forward. Meetings could be in-person or online at this point, depending on your preference. Also, CC'ed here is Dr. Tim Salcudean who will be the faculty supervisor for the team and oversee their engineering design process.

We provide significant leeway to clients and students to best determine how they would like to work together, but we suggest trying to meet as soon as possible to kick off the project. If, at any point during the project, you have any concerns or you would just like to check in, please feel free to contact me or Tim Salcudean.

Thank you for supporting the students by proposing this project. I will follow up in a later email to sort out signing the IP and NDA agreements.

We're looking forward to working with you!

Cheers,
Robyn

CUI, LUMENG <lumeng.cui@siemens-healthineers.com>

To: UBC-SBME Capstone; alykhan5@student.ubc.ca; tims@ece.ubc.ca

Cc: MORAN, GERALD <gerald.moran@siemens-healthineers.com>; **+1 other**

Wed 9/18/2024 15:09

[CAUTION: Non-UBC Email]

Hi Robyn,

Thank you very much. And glad to meet everyone here!

Please also meet my colleagues Dr. Jerry Moran (Research Collaboration Manager in Canada) and Dr. Stefan Sommer (MR Collaboration Scientist / Sequence Developer from Switzerland) for communication. I will be working with the team locally and closely in Vancouver, but Jerry and Stefan will also be involved with the project to provide any necessary support remotely.

I would like to invite Jerry and Stefan to the kick-off meeting to make sure we are on the same page in terms of goals and mutual expectations. Let me work out a schedule and agenda with them first, and I am hoping that we could have an online meeting some time next week. We will get back to you on this.

Looking forward to working with everyone!

Best,
Lumeng

CUI, LUMENG<lumeng.cui@siemens-healthineers.com>

To: MORAN, GERALD <gerald.moran@siemens-healthineers.com>; alykhan5@student.ubc.ca; **+1 other**

Wed 9/25/2024 09:24

You forwarded this message on Wed 9/25/2024 15:40

[**CAUTION:** Non-UBC Email]

Hi All,

We will have our first meeting to kick off the project. The goals of this meeting are,

1. Introduce the teams;
2. I will give some background introduction;
3. Set clear goals and expectations mutually;
4. For questions.

Please feel free to forward the meeting invite to anyone who would like to attend the meeting.

Thanks,

Lumeng

Lumeng Cui, Ph.D.

MR Collaboration Scientist

alykhan5@student.ubc.ca

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; **+2 others**

Wed 9/25/2024 12:46

Hello Lumeng,

Thank you for sending in the invitation. I am pleased to confirm that our team is available for the meeting between 12:00 and 13:00 PST on Thursday, 26th September.

We would also like to suggest the following items for discussion during the meeting:

- Potential use of AI in the project
- Signing an NDA (if needed)
- Possible alternative solutions to the problem
- Access to computing infrastructure, existing literature and datasets
- Meeting frequency
- Timelines for major deliverables

Kindly note that I will be forwarding the invite to other members of the team as well.

I sincerely appreciate your support on this project and we are extremely excited to meet with you and your team soon!

Regards,

Aly Khan Nuruddin [He/Him/His]

MG

MORAN, GERALD<gerald.moran@siemens-healthineers.com>

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; alykhan5@student.ubc.ca; **+1 other**

Thu 9/26/2024 13:05

Cc: Tim Salcudean <timsalcudean@gmail.com>; Jackson Chen <jacksonchen1196@gmail.com>; **+1 other**

[CAUTION: Non-UBC Email]

https://www.siemens-healthineers.com/magnetic-resonance-imaging/clinical-specialities/synthetic-ct

https://www.nature.com/articles/s41598-024-59014-6

Gerald R. Moran, Ph.D.
Research Collaboration Manager

---

alykhan5@student.ubc.ca

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To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; **+2 others**

Thu 9/26/2024 15:12

Cc: Tim Salcudean <timsalcudean@gmail.com>; Jackson Chen <jacksonchen1196@gmail.com>; **+2 others**

Capstone Team #17 - AI App... 146 KB

Client Meeting #1 - Minutes.... 155 KB

2 attachments (300 KB) Save all to OneDrive - UBC Download all

Hello Dr. Lumeng & Dr. Gerald,

Thank you for taking the time to meet with us today as well as for sharing your slides. We sincerely appreciate your support on this project and are excited to work with your team over the term.

Attached, kindly find a copy of our Meeting Minutes with documentation of the main talking points, expectations and deliverables for next week. I have also included the AI Approval Form for your perusal which is due tomorrow, Friday, September 27th. Please feel free to provide your feedback as well as your signature, which we would require for submission.

Our group was also wondering whether you would be comfortable with us presenting in front of our fellow capstone students or the general public. We would need to relay this information to the Capstone Team prior to signing the NDA.

We eagerly look forward to meeting with you next week.

Sincerely,
Aly Khan Nuruddin [He/Him/His]

TS

Tim Salcudean<tims@ece.ubc.ca>

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; alykhan5@student.ubc.ca; **+1 other**

Thu 9/26/2024 22:01

Cc: tims@ece.ubc.ca; Tim Salcudean <timsalcudean@gmail.com>; **+3 others**

Here are more papers that you may want to glance at.
Best,
Tim

https://www.ajnr.org/content/45/9/1284.abstract
https://ieeexplore.ieee.org/abstract/document/10635176?casa_token=tzUOYUbbgx4AAAAA:hE3eiNzn_1rfgC2isQfNEt48OJtJs8yny3Ibzr0tPjEgycDV9XlLrv7BTG1TrYYifSLjb1FFzw
https://www.sciencedirect.com/science/article/abs/pii/S1076633224006160
https://onlinelibrary.wiley.com/doi/full/10.1002/mrm.30275
https://link.springer.com/article/10.1007/s00330-023-10302-1

...

CL

CUI, LUMENG<lumeng.cui@siemens-healthineers.com>

To: alykhan5@student.ubc.ca

Fri 9/27/2024 09:50

Cc: MORAN, GERALD <gerald.moran@siemens-healthineers.com>; **+2 others**

[**CAUTION:** Non-UBC Email]

Hi Aly,

In terms of your question about whether we would be comfortable with you presenting in front of your fellow capstone students or the general public, in general yes, but we request that you double check with us for each instance.

It would be appreciated if we can review before you present any work, so that we can give suggestions or our thoughts, and ensure that any mention of Siemens tools or products is referenced appropriately. We anticipate that we can deal with this in a case-by-case manner instead of giving a general permission or prohibition right now.

We understand that something like this is required for your course, so we definitely don't want to refrain you from presenting your work, and we will do our best to respond to such requests quickly.

Also in case you need to fill out this info somewhere, the legal corporation name of Siemens Healthineers in Canada is "Siemens Healthcare Limited".

Please let us know if you have any further questions.

Lumeng

MG

MORAN, GERALD<gerald.moran@siemens-healthineers.com>

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; alykhan5@student.ubc.ca; **+2 others**

Thu 10/24/2024 12:50

Cc: Sommer, Stefan <sommer.stefan@siemens-healthineers.com>; **+2 others**

whitepaper-mr-only-rt-plann... 1 MB

siemens-healthineers-mreadi... 6 MB

2 attachments (8 MB) Save all to OneDrive - UBC Download all

[**CAUTION:** Non-UBC Email]

See attached

Gerald R. Moran, Ph.D.

Research Collaboration Manager

MG

MORAN, GERALD<gerald.moran@siemens-healthineers.com>

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; alykhan5@student.ubc.ca; **+2 others**

Thu 10/24/2024 12:56

Cc: Sommer, Stefan <sommer.stefan@siemens-healthineers.com>; **+2 others**

[**CAUTION:** Non-UBC Email]

Radiation Therapy

Gerald R. Moran, Ph.D.

Research Collaboration Manager

alykhan5@student.ubc.ca

Reply Reply all Forward

To: MORAN, GERALD <gerald.moran@siemens-healthineers.com>; CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; **+2 others**

Sat 10/26/2024 08:19

Cc: Sommer, Stefan <sommer.stefan@siemens-healthineers.com>; Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; **+1 other**

Capstone Team #17 - Semi-F... 840 KB

Capstone Team #17 - Client ... 129 KB

2 attachments (969 KB) Save all to OneDrive - UBC Download all

Hello Lumeng, Jerry & Everyone,

Thank you for taking out the time to meet with us this week and for providing us with the relevant resources.

Attached, please find the meeting minutes, as well as our presentation. As we were unable to fully cover the exploratory image analysis section on Slide #15, I have listed below the questions that our group had pertaining to the image processing techniques:

- How exactly might histogram equalization be used in our workflow processes?
- Do you have any recommendations on how to incorporate rigid/non-rigid transformations in our implementation?
- What might be other important image analysis techniques we could explore?

Kindly note that I have also been in touch with the teaching team and am awaiting to hear back from them about our availability for the meeting this coming Thursday.

Additionally, we will be working on fleshing out our ideas for the concept generation presentation. Please let us know whether it would be convenient for us to share our work with you for feedback early next week.

Hope you have a great weekend!

Thanking you in anticipation.

Sincerely,
Aly Khan Nuruddin [He/Him/His]

CL

CUI, LUMENG<lumeng.cui@siemens-healthineers.com>

To: alykhan5@student.ubc.ca; **+3 others**

Mon 10/28/2024 15:40

Cc: Sommer, Stefan <sommer.stefan@siemens-healthineers.com>; **+2 others**

[CAUTION: Non-UBC Email]

Hi Aly,

Thanks. Feel free to send over your slides to be presented for feedback.

Regarding your questions:

1. Regarding the histogram, have a look at these two papers for the idea. In general, we wanted a histogram-based thresholding, just like the idea stated in these two papers. I hope this can clarify our goals
   a. https://onlinelibrary.wiley.com/doi/10.1002/mrm.25545
   b. https://jnm.snmjournals.org/content/56/3/417.long
2. Registration (rigid/non-rigid) may help in the final evaluation step. I think we should prioritize other processing steps like n4-bias correction (i.e. image intensity equalization) and Histogram-Based Intensity Correction. I think 3D slicer might already have those functions readily available. Perhaps just read through these papers, and load the UTE images into 3D slicer and see if you can reproduce the results presented in the paper. In the end, we would want to implement these processing steps into coding. Once you get these steps done, the importance of registration will make more sense to you.
3. See the above.

Lumeng

CUI, LUMENG<lumeng.cui@siemens-healthineers.com>

To: alykhan5@student.ubc.ca; **+3 others**

Wed 10/30/2024 23:09

Cc: Sommer, Stefan <sommer.stefan@siemens-healthineers.com>; **+2 others**

Capstone Team #17 - Conce... 731 KB

UBC Capstone Project - shar... 3 MB

2 attachments (4 MB) Save all to OneDrive - UBC Download all

[CAUTION: Non-UBC Email]

Hi Aly,

Thanks for the presentation.

Some general comments:

1. I think your function structure diagram needs to be changed. I have put some detailed comments inside. The diagram I presented in our first meeting is a complete idea, and you can of course add your thoughts and ideas there but let's not make it too complicated and deviate our initial goals. People are going to have questions regrading this diagram as you have put many functions inside. I would suggest you to adapt the diagram from our first meeting and explain the idea to the audience in a concise way.
2. The concepts your presented are mostly ML based models. Make sure you explain them well and think about a solid response to answer how do them fit in this project.
3. Last but not the least, I would like to reiterate that our expectation is to develop a robust automatic workflow that converts UTE to pCT. We will leave you some room to be creative (e.g., ML/DL), but this to us is the icing on the cake. We are always ready to be impressed, but let's also aim to finish the project smoothly.

Great work and good luck with the presentation.

Best,

Lumeng

alykhan5@student.ubc.ca

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; **+3 others**

Thu 10/31/2024 11:19

Cc: Sommer, Stefan <sommer.stefan@siemens-healthineers.com>; **+2 others**

Hello Lumeng,

Thank you for your prompt feedback and invaluable advice, which I have shared with the rest of the team.

With regards to the Function Structure Diagram, I have made the necessary changes to more accurately reflect the scope of the image processing required for this project. Kindly find attached the image below, for your reference.

Additionally, your comments about the expectations for the workflow have been noted and we plan to stick to the outlined requirements while transitioning into the implementation phase for our solution.

Lastly, please let me know whether it would be convenient for us to meet next week so we can coordinate a time for Thursday.

Once again, thank you for all your support!

Regards,

Aly Khan Nuruddin [He/Him/His]

alykhan5@student.ubc.ca

Reply Reply all Forward ...

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; tims@ece.ubc.ca; Tim Salcudean <timsalcudean@gmail.com> Fri 11/15/2024 17:36

Cc: MORAN, GERALD <gerald.moran@siemens-healthineers.com>; **+3 others**

Delso G. et al. - Clinical Evalu... 2 MB

Wiesinger F. et al - Zero TE ... 2 MB

Capstone Group #17 - Literat... 467 KB

3 attachments (4 MB) Save all to OneDrive - UBC Download all

Hello Lumeng,

I hope that you are doing well.

Our group has prepared the following presentation, which outlines our progress over the past week. The attached document covers our key findings from the two papers provided, the transformations performed in ImageJ and 3D Slicer, as well as a review of possible approaches to image manipulation using code. I have also included the annotated literature below.

Kindly note that the team struggled with performing segmentation through both software tools. Additionally, the output achieved for bias correction through ImageJ was implemented via Gaussian Blurring since the N4ITK module was unavailable, although the result obtained did not seem to be correct.

Our team would look further into the above two issues and report back with any progress. Feel free to let us know if you have any suggestions in this regard.

On a positive note, we were able to perform the inverse logarithmic scaling successfully using Python code, and have developed a better understanding of the project requirements through the literature given.

We would be moving forward with implementing the bias correction via programming, and following up on concept generation with scoring and screening. Kindly note that our current Deep Learning approaches, as highlighted in the previous presentation are: (1) Generative Adversarial Networks (2) Random Forests (3) Convolutional Neural Networks (4) Random Forests and (5) UNet Architecture.

We eagerly look forward to meeting you next week and thank you for your guidance.

Sincerely,
Aly Khan Nuruddin [He/Him/His]

alykhan5@student.ubc.ca

Reply Reply all Forward ...

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; tims@ece.ubc.ca; Tim Salcudean <timsalcudean@gmail.com> Wed 11/20/2024 15:28

Cc: MORAN, GERALD <gerald.moran@siemens-healthineers.com>; **+3 others**

Hello Lumeng,

Hope this email finds you well.

I am writing to provide another update about our progress with the Capstone Project. As you are aware, last week we engaged in prototyping of the automatic image processing module and were successful in implementation of the inverse logarithmic scaling.

So far, our group has undergone concept generation for the Deep Learning component of the image background segmentation, selecting the following 5 options:
1. Generative Adversarial Networks (GANs)
2. Random Forests
3. Convolutional Neural Networks (CNNs)
4. Ensemble Methods
5. UNet Architecture

After our initial screening using a Pugh chart, we identified the GANS, Ensemble Methods and UNet Architecture.to be the most promising concepts. We further explored specific models, listed as follows, to proceed towards the scoring phase:
1. Multi-Cycle GAN
2, Stacked GAN
3. Attention UNet
4. Grad-CAM Guided U-Net
5. Ensemble Methods

We would love to share our work with you at tomorrow's meeting and would appreciate any feedback or advice before finalizing our concepts.

Thanking you in anticipation and looking forward to the meeting.

Best,
Aly Khan Nuruddin [He/Him/His]

alykhan5@student.ubc.ca

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; tims@ece.ubc.ca; Tim Salcudean <timsalcudean@gmail.com>

Cc: MORAN, GERALD <gerald.moran@siemens-healthineers.com>; Sommer, Stefan <sommer.stefan@siemens-healthineers.com>; **+2 others**

Reply | Reply all | Forward | ...

Fri 11/22/2024 20:06

Capstone Team #17 - Literat... 4 MB

Capstone Team #17 - Client ... 211 KB

2 attachments (4 MB) Save all to OneDrive - UBC Download all

Hello Lumeng,

Hope this email finds you well.

Thank you for taking your time to meet with our team and for providing your valuable feedback. Enclosed, please find our presentation slides as well as the Meeting Minutes.

I am also including below a breakdown of our 15 minute Critical Function Prototype (CFP) presentation, which is scheduled next week at 11:00AM on Thursday, November 28th:

- CFP selection
    - Which concept(s) will you be testing at this stage? Describe and justify.
    - What is the key question your CFP is intended to answer? Justify the importance/priority of this question. This may be one of your specifications, or part of your concept that you are least certain of.
- CFP Test Design
    - Choice of verification (or acceptance) criteria for CFP
    - Mapping of CFP features to verification criteria
    - Explanation of test protocols
    - Articulation of assumptions, scope of testing, limitations
- CFP demonstration
- Results – what did you find?
- Conclusions & next steps - what are your lessons learned?

With reference to the testing, we plan to compare the output obtained from the chicken dataset using our code. Hence, we would greatly appreciate if you could kindly provide the complementary CT images for the 3 MRI chicken images as that would significantly improve the robustness of our verification process.

Our team would be available to meet with you on Tuesday during our studio block between 11:00AM and 1:00PM. In this regard, please let us know whether this time would work for you, and feel free to suggest any alternative time slots, otherwise.

Looking forward to hearing from you soon.

Thanking you in anticipation.

Sincerely,
Aly Khan Nuruddin [He/Him/His]

---

alykhan5@student.ubc.ca

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; **+3 others**

Cc: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; Sommer, Stefan <sommer.stefan@siemens-healthineers.com>

Reply | Reply all | Forward | ...

Sun 1/19/2025 21:19

Capstone Team #17 - Client ... 161 KB

Hello Lumeng,

Thank you for taking out the time to meet with the team on Thursday.

As mentioned in the meeting, our group is currently looking to optimize the hyperparameters associated with the preliminary workflow before engaging in the deep learning. Based on the papers that you have provided and through our own research, we would be looking into implementation of different methods for the bias correction, inverse logarithmic scaling, and segmentation components.

In the meantime, we would be extremely grateful if you could provide us with better datasets for training of the machine learning pipeline following consultation with your colleagues.

Our group was also wondering whether you would be comfortable with us presenting in front of our fellow capstone students for the next round of presentations and in front of the general public on Design & Innovation Day.

Thank you for all your support and we look forward to discussing our findings with you next Thursday.

Sincerely,
Aly Khan Nuruddin [He/Him/His]

Niranjan Venugopal<nvenugopal@cancercare.mb.ca>

To: alykhan5@student.ubc.ca; Tim Salcudean <tims@ece.ubc.ca>; Asieh Tavakol <tavakol1@myumanitoba.ca>

Mon 1/20/2025 06:54

[CAUTION: Non-UBC Email]

Dear Tim and Aly,

Thanks for looping me into the conversation.

Aly, when you have a moment can you please give me a bit more details as to what your're looking for. We have an open source data set from the Synthetic CT challenge, but that data set does not contain UTE images. But it might be useful in general, for development and testing.

Please let me know if we can be of assistance.

Cheers,
Niranjan

alykhan5@student.ubc.ca

Reply Reply all Forward

To: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; Tim Salcudean <tims@ece.ubc.ca>; **+1 other**

Wed 1/22/2025 21:03

Hello Niranjan,

Thank you for reaching out to us about the dataset.

Our group is currently looking into alternative methods to improve the robustness of our existing pipeline for UTE-MR to synthetic-CT conversion with cortical bone segmentation. For the time-being, we are constrained to work with conventional modules such as N4ITK, SimpleITK etc., due to the limited access to clinical data. Hence, it has been a challenge for the group to incorporate deep learning methods into the image processing workflow.

Additionally, we currently do not have access to the gold standard CT scans for the chicken dataset, so are unable to use metrics such as the DICE, SSID etc. to make comparisons with our pseudo-CT output.

We would greatly appreciate any support or insights that you may have on this matter.

Please feel free to reach out if you have any further questions.

Thanking you in anticipation.

Regards,
Aly Khan Nuruddin [He/Him/His]

CUI, LUMENG<lumeng.cui@siemens-healthineers.com>

Reply Reply all Forward

To: alykhan5@student.ubc.ca; tims@ece.ubc.ca; MORAN, GERALD <gerald.moran@siemens-healthineers.com>; Asieh Tavakol <tavakol1@myumanitoba.ca>

Wed 2/19/2025 14:31

Cc: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; Sommer, Stefan <sommer.stefan@siemens-healthineers.com>

[CAUTION: Non-UBC Email]

Hi Aly,

Sounds good to me to reschedule the meeting.

I will send you some new data. Check your mailbox later.

In terms of the dataset for deep-learning, I suggest we should explore some open source datasets like this

https://github.com/ChengBinJin/MRI-to-CT-DCNN-TensorFlow?tab=readme-ov-file

It has paired MR and CT datasets although the MRI seems not to be the UTE data. But the goal is still the same, i.e., from MR to sCT. In theory, if you come up with something in the end, we can still potentially translate the method to UTE and CT.

Though we expected the non-AI method to be the pillar of the project, we understand the group's excitement about the AI method. I think this repo can be a nice example and starting point for you guys.

I wanted to highlight some points in terms of this:

1. The MR and CT dataset in this repo are paired, which save you the effort of registration.
2. The dataset size and complexity of this demo is right amount for you guys.
3. Primary goal for using this repo is to use the Open source toy dataset they provide to design your work and demo in the end; that said, you can still try to explore and run their code for the tutorial purpose.
4. Adding to Pt.3, we expect you to develop your own method.
5. Feel free to source any other open source datasets if you think you have better candidates.

Best,
Lumeng

...

alykhan5@student.ubc.ca

Reply Reply all Forward

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; Septimiu Salcudean; MORAN, GERALD <gerald.moran@siemens-healthineers.com>; **+1 other**

Thu 3/13/2025 10:27

Cc: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; Sommer, Stefan <sommer.stefan@siemens-healthineers.com>

Capstone Team #17 - Client ... 101 KB

Capstone Team #17 - Alpha-... 7 MB

2 attachments (7 MB) Save all to OneDrive - UBC Download all

Hello Lumeng,

I hope this email finds you very well and apologies for the delayed update.

Thank you for taking out your time to meet with our team last week and for sharing your feedback on our presentation. We sincerely appreciate all your support with our project.

Attached, please find our Presentation Slides and the Meeting Minutes for your reference.

As you are aware, our group had the opportunity to present our Alpha-Design Review to the teaching faculty on Thursday. In this regard, we received some valuable guidance that would shape our work over the course of the next few weeks:

- We were advised to refrain from showing live code as it can be distracting for the audience to follow. Instead, it would be more appropriate for us to showcase our results, visually. Hence, the group is exploring different ways to better present the information in a more structured manner. Currently, we aim to do so by following the template in Figure #2 of the following paper. We would be happy to discuss this further with you at our next meeting.
- Additionally, we were suggested to examine quantifiable metrics for comparison between the pseudo-CT and gold-standard CT images. Our team is looking at performing a one-to-one reference mapping for the MRI to the CT images to enable computation of metrics such as SSIM, MAE and DICE etc. that were highlighted in our evaluation criteria.
- Lastly, given the time constraints and lack of relevant open-source datasets, our group would be utilizing the remaining 3 weeks to validate and verify the performance of the non-AI pipeline instead of working on the deep learning as was our previous intention. We also want to leave some time for completion of the course documentation and to adequately prepare for our Poster Presentation at the Capstone Design & Innovation Day on Thursday, April 3rd.

Our team would also be very appreciative if we could meet bi-weekly instead for the remainder of the term. This would provide us with some room to complete our prototyping, consult with the teaching faculty and to integrate your feedback in a timely manner.

Hence, we look forward to meeting with you next week, on Thursday, March 20th. Please let us know whether 12:00PM would be a suitable time for you.

Thanking you in anticipation.

Regards,
Aly Khan Nuruddin [He/Him/His]

alykhan5@student.ubc.ca

Reply Reply all Forward

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; Septimiu Salcudean; Asieh Tavakol <tavakol1@myumanitoba.ca>; **+1 other** Thu 3/20/2025 13:01

Cc: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; Sommer, Stefan <sommer.stefan@siemens-healthineers.com>

Hello Lumeng & Everyone,

I hope this email finds you in the best of health.

We would like to share the exciting news that our group will be presenting at the UBC Applied Science Design & Innovation Day, 2025. This event will be a showcase of our Capstone Project to the general public and is scheduled for Thursday, April 3rd, from 2:00 to 5:00PM. For more information, please refer to this link: https://experience.apsc.ubc.ca/design-and-innovation-day

In this regard, we wish to extend an invitation on behalf of the team for you to join us at the event. We would sincerely appreciate your presence and support in-person, if convenient.

The team is currently working on consolidating the deliverables for the annual showcase which includes the following:

- **Abstract:** Provides a concise description of the project suitable for a general audience.
- **Visuals:** Showcase relevant input MR images, corresponding pseudo-CT output scans and comparative gold-standard CT images to establish the utility of our design solution.
- **Code Repository:** Demonstrates the operability of our working digital program.
- **Poster:** Captures the motivation for tackling the problem space in healthcare, depicts our innovative imaging prototype, and details its impact within the domain of clinical diagnostics.

We would be very grateful if you could kindly grant us your permission to present this material at the Design & Innovation Day. As always, the team will do their due diligence in sharing all the information above before the event.

Hence, we would be very grateful for your support and consideration in this matter.

Looking forward to hearing form you soon.

Sincerely,
Aly Khan Nuruddin [He/Him/His]

CL

CUI, LUMENG<lumeng.cui@siemens-healthineers.com>

To: alykhan5@student.ubc.ca; Septimiu Salcudean <tims@ece.ubc.ca>; **+2 others** Fri 3/21/2025 09:17

Cc: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; **+1 other**

[**CAUTION:** Non-UBC Email]

Hi Aly,

We understand this is part of your course requirement and grading, and you have our permission to present the work.

Thank you.

Best,
Lumeng

alykhan5@student.ubc.ca

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; Septimiu Salcudean; **+2 others**

Wed 3/26/2025 13:44

Cc: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; Sommer, Stefan <sommer.stefan@siemens-healthineers.com>

Capstone Team #17 - Poster ...
987 KB

Hello Lumeng,

I hope this email finds you well.

The team has prepared the following poster for presentation at our upcoming Design & Innovation Day, 2025.

We would greatly appreciate if you could kindly provide your feedback on the attached poster by the **end of day** as our deadline for submission is 9:00AM tomorrow. Please note that some modifications to the results section are still pending.

Sincere apologies for the short notice and thank you for your consideration.

Regards,
Aly Khan Nuruddin [He/Him/His]

CL

CUI, LUMENG<lumeng.cui@siemens-healthineers.com>

To: alykhan5@student.ubc.ca; Septimiu Salcudean <tims@ece.ubc.ca>; **+2 others**

Wed 3/26/2025 14:40

Cc: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; Sommer, Stefan <sommer.stefan@siemens-healthineers.com>

[**CAUTION:** Non-UBC Email]

Hi Aly,

Good job, and here are my suggestions:

1. Can you please swap the Knee dataset with the Ankle data I sent you last week? This knee is not the best example to showcase, and the ankle should be more appropriate.
2. I would break Figure 4 into two figures. The chicken dataset should be used to highlight the side by side comparison to demonstrate the workflow works. And it should be presented with the histogram in Figure 5.
3. Supposing the workflow has been proved valid by this chicken dataset/result, then in the next Figure, it would be a good idea to present how it works with a real-life in vivo dataset where the ankle data should come in. We couldn't provide you CT ankle along with it, but you can use arrows to highlight the bone contrast etc (to echo with your background and problem section).
4. Figure 2 in the background, Figure 3 in the Existing Solution, and the figure in proposed solution are from the literature, make sure you make that clear and put references next to them (you can find the references from the kick-off slides I shared with you).
5. Please leave St. Paul's Hospital logo out of the poster as they are not directly involved.
6. In the acknowledgement section, I would include everyone here in this email thread.

Let me know if any piece (e.g., data/slides) is missing on your end, I can resend.

Once finished, I would appreciate if you can send us the polished version.

Good luck on your submission.

Lumeng

TS

Tim Salcudean<tims@ece.ubc.ca>

To: alykhan5@student.ubc.ca; CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; **+2 others**

Wed 3/26/2025 15:38

Cc: tims@ece.ubc.ca; Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; **+1 other**

Capstone Team #17 - Poster ...
998 KB

I have attached feedback on your poster - TS

...

alykhan5@student.ubc.ca

To: Septimiu Salcudean; CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; **+2 others**

Thu 3/27/2025 10:46

Cc: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; Sommer, Stefan <sommer.stefan@siemens-healthineers.com>

Capstone Team #17 - Poster ...
927 KB

Hello Everyone,

Thank you for your valuable input on our poster presentation. Attached, please find the finalized version with the requested changes incorporated for your consideration.

We look forward to presenting our work to the SBME community next week.

Additionally, our group had the following questions regarding the validation of our software prototype:

1. How shall we downsample the CT image on 3D slicer? Our team was not getting the expected results here.
2. How shall we accurately resample the CT volume to match the MRI for registration?

We would also greatly appreciate your assistance and clarification in this matter.

Thank you for your support.

Sincerely,
Aly Khan Nuruddin [He/Him/His]

---

alykhan5@student.ubc.ca

To: CUI, LUMENG <lumeng.cui@siemens-healthineers.com>; Septimiu Salcudean; **+2 others**

Sat 4/5/2025 20:52

Cc: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; Sommer, Stefan <sommer.stefan@siemens-healthineers.com>

Capstone Team #17 - Client ... 128 KB | NASA TLX Scale.pdf 8 KB | Client Check-off Form.docx 56 KB

3 attachments (193 KB) Save all to OneDrive - UBC Download all

Hello Lumeng & Tim,

Thank you for taking the time to meet with our group earlier this week. Attached, please find the meeting minutes.

Our poster presentation at Design & Innovation Day on Thursday went really well! We sincerely appreciate all the support that you have provided to get us to this stage.

Currently, our team is looking into the image registration process to obtain the quantifiable metrics for design verification. For the client validation, we would be very grateful if you could evaluate our codebase on the NASA TLX Scale provided, as well as complete the Client Hand-Off Form, preferably by Tuesday, April 08th. The GitHub link is as follows: https://github.com/Yakuson/MRI-TO-PCT/tree/main

Our next deadline is on Friday, April 11th, for submission of the Final Report. We will share the documentation and repositories with you for your reference prior to completion of the course deliverables.

Feel free to reach out if you have any questions.

Looking forward to hearing from you soon.

Regards,
Aly Khan Nuruddin [He/Him/His]

CUI, LUMENG<lumeng.cui@siemens-healthineers.com>

To: alykhan5@student.ubc.ca; Septimiu Salcudean <tims@ece.ubc.ca>; **+2 others**

Sun 4/6/2025 17:40

Cc: Niranjan Venugopal <nvenugopal@cancercare.mb.ca>; **+1 other**

Client Check-off Form_LC Sig...
182 KB

NASA TLX Scale_LC.pdf
15 KB

2 attachments (197 KB) Save all to OneDrive - UBC Download all

[CAUTION: Non-UBC Email]

Hi Aly,

Glad to hear! It has been a pleasant journey.

I hope you guys all succeed and have a bright future.

Best Regards,
Lumeng

M2.3.2. Memorandums

Hello Dr. Cui & Dr. Moran,

Thank you for taking the time to meet with us today as well as for sharing your slides. We sincerely appreciate your support on this project and are excited to work with your team over this term.

The following paragraph is a brief summary of our meeting today:

<u>Meeting Summary:</u>
Today's meeting, held on Thursday, September 26th, from 12:00 to 13:00 PM, was the first interaction between Team #17 and our client, Siemens Healthineers, Canada. The meeting began with introductions of the UBC Capstone Team: Aly Khan Nuruddin, Lynn Alvarez Krautzig, Manan Verma, Yuheng Zhang, and Jackson Chen, followed by introductions from our Supervisor, Tim Salcudean, and the Siemens Team: Lumeng Cui and Gerald Moran. Next, the client presented an overview of the project, highlighting key differences between the two imaging modalities of Magnetic Resonance (MR), and Computerized Tomography (CT). The main goal of the project is to design an automatic image-processing prototype using Ultrashort Echo Time (UTE) MRI to synthetic CT images. The first task of the design involves implementing computerized techniques such as bias correction, inverse logarithmic-scaling, and image background segmentation to obtain the output images. The second task is optional and considers deep learning methods to further enhance bone contrast, which will be tested using in vivo and in vitro datasets. The client then discussed miscellaneous items like expectations and frequency of meetings, while addressing the selection of development tools and resources for research literature. Finally, a set of tasks was outlined to be completed prior to our next meeting on Thursday, October 3rd, following which the floor was opened to questions. Our team then gathered information about the permissible use of AI, terms of a non-disclosure agreement (NDA), as well as possible computing infrastructure required to produce the deliverables. Overall, the meeting was productive and formally kicked-off our engagement with the client.

Additionally, attached kindly find a copy of our Meeting Minutes with documentation of the main talking points, expectations and deliverables for next week. I have also included the AI Approval Form for your perusal which is due this Friday, September 27th. Please feel free to provide your feedback as well as your signature, which we would require for submission.

We eagerly look forward to meeting with you next week.

Sincerely,
Aly Khan Nuruddin (Client Liaison - Team #17)
Hello Dr. Cui & Dr. Moran,

Thank you for taking out your time to meet with our team and for sharing your insights on our image processing prototype. We sincerely appreciate all your support on the project so far.

The following paragraph will provide a brief summary of the work performed by the team to date while outlining subsequent steps for iterative design and consolidation into a working pipeline:

<u>Summary of Alpha-Design</u>
Our current prototype inputs Magnetic Resonance (MR) images acquired using an Ultrashort Echo-Time (UTE) sequence and outputs its corresponding pseudo-Computed Tomography (pCT) scans. First, the UTE-MR images undergo inverse-logarithmic scaling to enhance cortical bone contrast with intensity normalization for cross-modality comparison. Next, a histogram-based bias correction technique is applied to adjust signal inhomogeneities using the N4ITK module in tandem with manual hyperparameter optimization to yield the sharpest histogram peaks. Subsequently, an automatic thresholding method is implemented with morphological closing to speed up the downstream design process for image segmentation. However, prior to this module, Gaussian fitting is utilized to compute the upper and lower thresholds using the full-width half-maximum of the signal and noise peaks. Correspondingly, the generated segmented images retain contrast between cortical bone and soft-tissue while aptly removing background noise. The value proposition of the imaging pipeline is to provide supplementary diagnostic information to radiologists through an alternative modality like pCT while using existing MRI machines.

Attached kindly find a copy of our Meeting Minutes with documentation of the main talking points, expectations and deliverables for next week. Additionally, I have included our Progress Update Presentation which highlights our most up-to-date results for your kind perusal.

In this regard, our group would be eager to arrange for a meeting to review the design. This would provide us with the opportunity to formally present our comprehensive device and to obtain your constructive feedback on the technical robustness of our software product.

We would be very grateful if you could please let us know your availability for the month of March to schedule an hour-long meeting so we can showcase our design to you and your team.

Eagerly looking forward to hearing from you soon and thank you in advance.

Sincerely,
Aly Khan Nuruddin (Client Liaison - Team #17)

M2.3.3. Meeting Minutes

Client Meeting #1.

Summary:

Siemens Healthineers Canada is a subsidiary of Siemens AG, a global technology company with products and services in various markets. Siemens Healthineers Canada's main focus is to deliver innovative solutions to healthcare providers, ranging from medical imaging to laboratory diagnostics. The primary client for this project is Dr. Lumeng Cui, an MR collaboration scientist working for Siemens Healthineers Canada.

The project provided by the client aims to create an automated image processing software to produce pseudo-computed tomography (pCT) from Ultrashort Echo Time (UTE) Magnetic-Resonance (MR) images. Radiation Therapy (RT) for cancer patients requires imaging to aid in the development of a treatment plan to target the malignant tissue effectively. While CT images are commonly used in RT, over the past few years, there has been research in assessing the potential of MRI to achieve improved clinical outcomes. MRI has superior soft-tissue contrast which can help improve localization accuracy. However, MRI has limitations in imaging the cortical bone. One technique aimed at overcoming this challenge is UTE.

Producing pCT from UTE-MR images could help give healthcare providers with adequate alternatives to current, standard imaging protocols for RT treatment plans.

Questions:

- Would you be comfortable with us presenting in front of our fellow capstone students or the general public? (To what extent is this project proprietary, and which aspects of the project should we take extra care to avoid divulging?)
- What tasks would be appropriate to use AI tools for and are there any pitfalls/limitations we should be aware of?
- What are some regulatory obstacles that need to be considered for design of our solution?
- What is the biggest problem encountered by medical radiation technologists and/or radiologists while using MRI for cortical bone imaging?
- What post-processing techniques would facilitate improved image contrast?
- What are some softwares or technologies that would be useful for the project?

Date: Sept. 26, 2024

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Gerald (Jerry) Moran, Lumeng Cui
- *Faculty Supervisor:* Tim Salcudean

Meeting Agenda:
- AI Approval Form - Deadline Friday, September 27th
- NDA
- Access to Existing Literature & Datasets
- Access to Computing Infrastructure
- Alternative Solutions
- Meeting Frequency
- Timeline for Major Deliverables

Meeting Minutes

Topic 1: Introductions of Both Teams
- Capstone team
- Siemens team:
  - Jerry Moran
    - Head of research for Siemens Canada, MRI branching out into CT/PET
  - Lumeng Cui
    - MR Siemens collaborative scientist, supporting St.Paul's Hospital
    - UTE, image processing, and spectroscopy
    - Background in biomedical engineering, master in elastography from University of Saskatchewan
    - Globally responsible for spectroscopy
    - Supports customers in Canada and abroad
- Faculty supervisor
- Note: Stephan Sommer, MR scientist will join subsequent meetings

Topic 2 : Project Overview & Background
- Project goal:
  - Design automatic image processing prototype using UTE to generate sCT
- MR provides superior soft tissue contrast and is mainly used for tumor detection, therapy, and disease diagnosis

- CT better bone visualization modality and provides dose information for radiation therapy
- CT carries radiation, making MR safer
- When trying to collect MR images, some tissues have a short T2 signal that will decay before it can be recorded
- Conventional MR has drawbacks where certain regions such as cortical bone, tendon or meniscus show up as dark areas
- Advantages and disadvantages of both MR & CT - would be good to combine their strengths together
- Bone-air visualization is the tricky part, cannot separate them in MR
- UTE MRI can directly image the bone without any intensity conversion, eliminating the bone-air separation issue
- UTE MRI images can be converted into CT-like images

Topic 3: Project Design

- Task 1: Design an automatic image processing program with the steps:
    - Bias correction (correct signal inhomogeneity)
    - Inverse logarithmic rescaling for enhancing bone contrast
    - Image background segmentation (Retain bone and soft tissue contrast and remove background air)

  Note: For Task 1, design an easy workflow without involving AI or deep learning.

- Task 2: (Time Permitting - Bonus)
    - Use deep learning
    - UTE MR images to train the network and then be provided with testing dataset for generating CT-like images
    - Datasets depend on the progress of the project for training of the network

Topic 4: Expectations

- Deliverable #1
    - Main deliverable: Task 1 is the main deliverable that is expected (Conventional Workflow)

- Deliverable #2
    - Depends on team motivation as well as progress made

- Do not share given data with others

- Development Tools

    - Not limited to particular tools
    - Suggestions:
        - Python, Github, Jupyter Notebook, ImageJ, 3Dslicer, Microdicom

- Literature
    - Can provide it but the team is expected to do their research
    - Encouraged to seek open-source solutions to address issues

- Meeting Frequency
    - Bi-weekly meeting with Dr. Lumeng Cui for 30 minutes for updates & questions
    - Bi-monthly meeting with bigger Siemens team

- Other
    - Must document the process for meetings, solutions, issues, questions, and action items for each team member
        - Eg: Can use tools like OneNote or Google Doc
    - For additional costs (i.e. poster print) and publications, let Jerry know in advance and can go over it later

- Future Possibilities
    - Siemens decided to go with an AI-based sCT product but the UTE sCT can potentially outperform current technologies with room to improve
    - Faster, easier workflow
    - What is meant by workflow?
        - One automatic program/prototype could be stand-alone or sit on an online interface like Open Recon
            - Ex. if given UTE images program can be run and results will be given
        - Input: UTE images
        - Output: Set of images that look like CT and can be imported into radiation workflow

Topic 5: Upcoming Deliverables

- Before next meeting on Thursday Oct. 3, 2024:
    - Share literature findings
        - See if open source image data sets can be found online
    - Decision on development tools selected and status of setup and configuration of computers
    - Ideas on the design of the prototype (As specific as possible)
    - Breakdown of the project and its timeline for each part

- Resources from client:
    - Can provide UTE images for task #1, CT images only needed for task #2
        - Set of images with both MRI and CT
            - Ensure we can examine them
            - Will be given ASAP
            - Know how to work with Dicom
        - Separate different tasks and discuss findings within the team
        - Faculty supervisor may be able to get CT scans for team to use
    - Slide deck presented during meeting will be shared with references to get started on literature review
    - Shared links:
        - https://www.siemens-healthineers.com/magnetic-resonance-imaging/clinical-specialities/synthetic-ct
        - https://www.nature.com/articles/s41598-024-59014-6

Topic 6: Questions from Students

- AI Approval
    - No uploading images
    - No code generated from AI (Allowed for minor assistance)
    - Open-source package is fine but make sure that it is annotated in the code
    - Segment out section of the code generated by AI with adequate documentation as well

- NDA:
    - Waiting for the paperwork to come back from UBC so that it can be signed

- Computing Resources:
    - Personal laptops will be fine
    - Computing infrastructure is not needed as datasets are not that big

Table A6. *Action Items from the First Client Meeting.*

Actionable	***Persons Responsible***	***Deadline***
Progress Slides for Next Client Meeting	All	Tues. Studio Block (Oct. 1)
Decide on Computational Tools Required for Project		
Draft Ideas for Prototype Design		
Expand on Literature Findings (Open Source Images and Tools, State-of-the-Art Modalities, etc.)	Manan, Yuheng	
Download and Look into Medical Image Viewers	Lynn	
Generate Gantt Chart and Timeline	Aly Khan, Jackson	

Client Meeting #2

Date: October 3, 2024

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Gerald (Jerry) Moran, Lumeng Cui, Stephan Sommer, Asieh Tavakol, Niranjan Venugopal
- *Faculty Supervisor:* NA

Meeting Agenda:
- Presentation by Capstone Team:
  - Literature Findings
  - Project Timeline
  - Questions for Client

Meeting Minutes

Topic 1: Introductions

Asieh Tavakol
- Cancer Care Manitoba
- Using flexible UTE sequence for synthetic CT generation
- PhD student at the University of Manitoba
- Works as a medical physicist in radiation therapy

Stefan Sommer
- Focusing on UTE sequence and reconstruction
- Works together with Lumeng at Siemens, based in Switzerland
- Tried to do image translation from MR to CT

Niranjan Venugopal
- Medical physicist at the University of Manitoba
- Worked on developing novel techniques
- Using UTE information for developing sCT with applications in radiation oncology

Topic 2: Presentation Feedback
- ZTE is essentially the same thing as UTE, defines the center of timing so that there can be zero echo time **(different nomenclature)
- Deep learning and GAN are two very different models

        - Lots of data
        - Train in 2D or 3D
- Pre processing focused on bias correction and inverse logarithmic scaling (Gets an easy CT-like image)
- Might not have UTE MRI on open image sources
- Identify what is working well or not and what deep learning could help with
- Image segmentation should focus on bone/air separation (Can use histograms for thresholding) and segmenting foreground from background (Could be the most important or challenging aspect)
- Need: Identify where object is after inverse contrast and find proper boundaries
- Use phase imaging of UTE
- Project is not developed in three parts equally
    - Some parts will be more challenging or easier (i.e. image rescaling can be quite easy)

Topic 3: Questions for the Client

- What do you recommend we use the budget on?
    - Access to GPUs for the deep learning aspect
        - Cloud credits
    - If the budget exceeds the limit, it can be approved by the Siemens team

- What are some regulatory obstacles?
    - If an algorithm is trained on public data, the license agreement of the public data should be checked to see if it can be used in commercial settings

- Is there a particular tissue we should be focusing on?
    - The given data will be mainly short T2 tissues (i.e. cortical bone) imaged using UTE
    - Once it is trained we can look into other tissues and retrain the model
    - Asieh has a slide deck highlighting the issues - which may be presented in the next client meeting
    - One of the main problems is that current sCT doesn't do well in capturing bone-soft tissue interfaces and bone-air interfaces
        - Some algorithms produced "hallucinations" (artifacts)
        - The current algorithm is trained by specific MR techniques (ex. T1 weighted) for clinical applications
    - UTE technique can create contrast between the bone and air
        - For brain, this can be an issue due to air space in the nose

- What pre-processing and post-processing techniques should we look into?
    - Bias field correction can help with intensity for pre-processing of images
    - Open to try new processing techniques to improve workflow
        - I.e. come up with our own bias field correction
    - Important to be generalized for many cases
        - Ex. if healthy images are only used to train it can create bias when an unhealthy image is brought on
        - Ex. Had to remove parts of a skull for brain imaging and the model added the skull back as an example so segmentation of the pathology is important
    - In UTE there is some physics differentiating between bone and air

- Siemens already has a sCT AI-based product, what are the shortfalls?
    - Shortfalls:
        - Has been trained on conventional MR images, which cannot differentiate bone and air
        - Not best in terms of resolution (good resolution can go down to 0.3mm)
    - Advantages:
        - Can provide HU units

    - Main Goal is to create a CT-like image with very high contrast between bone and the rest of the tissue and also bone and air (Get as close as possible and don't care about absolute values)
    - First goal is to try to create CT-like image from MR, if there is more time look into creation of sCT which requires the application of HU

- In terms of our approval form is there anything you could think of that would be beneficial for us to add?
    - Gantt chart could also be added into this

Topic 4: Questions from Clients

- Could we record the client meeting sessions?
    - Yes. We can record the client meeting sessions.

Topic 5: Final Remarks from Client

- UTE/ZTE/Petra are all similar but there are some minor differences
    - Don’t need to understand the physics behind
- Ni.gzz files will be given for the images

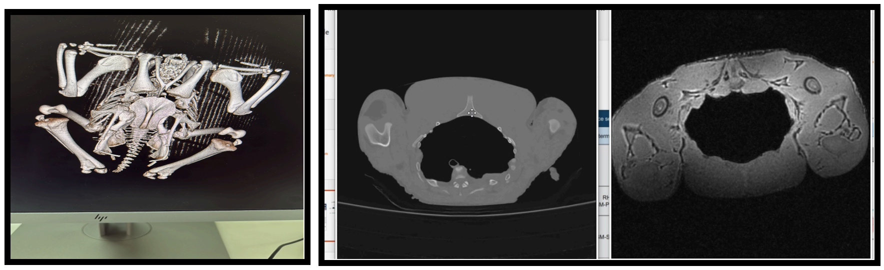

Figure A6. *CT Images of a Chicken Skull.*

Topic 6: Upcoming Deliverables

- Work on a dedicated budget, what is the best options
    - Buy GPU or Cloud Credit
    - If urgent: give a couple weeks heads up to Gerry
- Share feedback/questions on things noticed on the images provided
- Add to meeting minutes what deliverables will be done / presented by next meeting

Table A7. *Action Items from the Second Client Meeting.*

<table>
<tr><th>Actionable</th><th>Persons Responsible</th><th>Deadline</th></tr>
<tr><td>Explore Provided Dataset</td><td rowspan="3">All</td><td rowspan="4">Tues. Studio Block (Oct 08)</td></tr>
<tr><td>Questions for Client</td></tr>
<tr><td>Download Development Tools</td></tr>
<tr><td>Budget and Computational Resources (GPU, Cloud)</td><td>Yuheng, Jackson</td></tr>
</table>

Client Meeting #3

Date: October 10, 2024

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Gerald (Jerry) Moran, Lumeng Cui, Stephan Sommer, Asieh Tavakol,
- *Faculty Supervisor:* Tim Salcudean

Questions for the Client:
- What post-processing techniques were added to the corrected image?
- Are there any artifacts (features that do not correspond to the anatomy) present in the image?

Meeting Minutes

Topic 1: Updates for Client
- Our team has been working on getting DHF 1 completed for tomorrow
    - Stakeholder analysis, value proposition, alternative solution
    - Make presentation of DHF 1 progress for next meeting

Topic Questions for the Client
- What post-processing techniques were added to the corrected image given?
    - When UTE images are collected there is a lot of body fat inside the tissue which can create chemical shift artifact, in regular MR this can be fixed
    - UTE uses non-cartesian acquisition which can cause issues with the images
    - Suppress the fat signal and only collect the muscle and other tissues, if this is not corrected it can blur the image creating an off-resonance artifact
    - Given both, suggest using the uncorrected one for prototype
    - Post-processing in corrected image is an 'in-house' technique
    - Lumeng will try to find an example of the fat artifact and share
    - Techniques can be implemented in the acquisition

Topic 2: Questions from Clients
- Any issues regarding using Dicom or nifty?
    - Decided to go with 3D Slicer

- What is meant by smoothness?
    - Edges are defined better → Call this sharp instead of smooth

- CT can provide more resolution but we need to be aware of the contrast
- ‘Smooth’ has different meaning in imaging, we are looking for the sharpness hoping that the image can provide a lot of detail and diagnostic information
- Graininess corresponds to signal-to-noise ratio (SNR)

- What is registration?
    - When MR and CT are collected they are taken separately, although sometimes you want to match orientation and position to be as close as possible
        - In reality, this is not always possible
    - Image registration is used to overcome this
    - Look for a registration algorithm
        - Allow them to have same orientation and same position
        - This can help to evaluate the workflow
        - Some examples, many more to look at:
            - Rigid
                - Simple technique
                - Doesn’t matter which one you choose as template or moving image
            - Non-rigid
                - If MR is smaller than CT we can figure out how to scale
            - Elastic registration
                - More complex
                - Deform the MR image in certain way and get it to match up with the CT
    - 3D Slicer includes some registration module
    - There might even be methods that don’t require image registration
    - In BMEG 420 course (Medical Imaging) there is a basic introduction to registration and segmentation
        - Look at this for background knowledge
        - Learn how to subsample an image
            - Need to look at CT and bring it down to the same resolution, comparison is difficult when resolution is different
            - Rigid registration in slicer, routines available to do that
    - Do not start with massive non-rigid problem, could be complex
        - Begin with rigid registration
        - Qualitative evaluations of contrast with CT exist as mentioned in the papers provided
        - Robotics and introduction to computer vision (vision and control) textbook available (Robotics, Vision and Control: Fundamental Algorithms in MATLAB/Python - Peter Corke)

            - Examples in MATLAB and Python
            - 2 chapters corresponding to segmentation, image processing, registration etc.
        - Goal of the process is not to develop a good registration method
        - Trying existing methods will be sufficient
    - Do not spend too much time focusing on registration, find what is good enough
    - Certain steps are pretty standard/conventional
    - Look at histograms and see how values are distributed
    - While 3D Slicer can be used, it is important to go over basic image analysis to get a good understanding
    - Have a look at ImageJ, very fast and can directly load images
        - Lumeng has a lot of personal experience using it
        - Look at histogram and do simple processing like inverting contrast
            - i.e. Histogram equalization
        - Doesn't really matter which imaging tool, simply suggestions

Topic 3: Presentation from Asieh

- Challenges in AI based sCT for radiotherapy
    - sCT provides better soft-tissue visualization, eliminates registration uncertainties, reduces costs, and minimizes unnecessary radiation exposure
    - Technical issues:
        - MRI limitation: Has difficulty in separating bone air interfaces especially in sinus regions, causes mri signal to vary and makes it hard to distinguish.
        - Data mismatch: Differences in mri scanner models can lead to inconsistencies and not produce accurate results
        - Lack of standardization: no established QA protocols in hospitals which can result in inconsistencies
        - Data requirements: AI models require large diverse datasets, how we are acquiring the data is important + AI models need to perform consistently across all patient types and scenarios.
            - Ex. A model trained on the brain will have issues when implemented in a pediatric scenario.
        - Bone clarity & Mislabeling: Regions near air cavity, such as sinuses and bones, may not be clear and there may be tissue mislabeling
            - Ex. If soft tissue are near bone they are incorrectly labeled as bone
        - Implant interface: metal implants can lead to artifacts and inaccuracies in dosage calculation
            - Ex. metal implant in jaw could create "bone like structure"
    - The clarity of bone features may be degraded
    - Bony structures near air cavities are less detailed in sCT

    - DSC and MAE are mentioned
    - A, B, C on the last slide are different algorithms for generating sCT
        - A is better according to metrics
        - Sometimes when there are large air spaces, sCT might not perform as well
        - A only has been tried on pelvis and brain
        - A,B,C are publicly available data
    - Presentation will be shared

Topic 4: Upcoming Deliverables

- Go over rigid and non-rigid transformations, identifying which is better suited for the task
    - What methods are available and what did we miss today?
    - What aspect can help with these transformations?
    - Use the BMEG 420 textbook to read up on registration and segmentation (Fundamentals of Medical Imaging - Paul Seutens)
        - Take a look at Gaussian filter (how to visualize air between images)
    - Learn how to subsample an image and bring the resolution of a CT down to that of a MRI
    - Use rigid registration in 3D Slicer for this
- Explore the registration, segmentation and module finder features of 3D Slicer for automatic pipelines
- Explore ImageJ
- Try manipulating the chicken images
- Create slides for next meeting about what has been done, what will be done and questions for the client

Table A8. *Action Items from the Third Client Meeting.*

Actionable	***Persons Responsible***	***Deadline***
Read and Understand the Basics for Image Manipulations	All	Thurs. Studio Block (Oct 17)
Read Two Chapters of *Robotics, Vision and Control: Fundamental Algorithms in MATLAB/Python* - Peter Corke		
Explore ImageJ Software + Make Image Manipulations on 3D Slicer with Chicken Dataset		
Create a Presentation Outlining Progress and Go Over Listed Actionable Items		

Client Meeting #4

Date: October 24, 2024

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Gerald (Jerry) Moran, Lumeng Cui, Asieh Tavakol
- *Faculty Supervisor:* Tim Salcudean

Meeting Minutes

Topic #1: Comments about Presentation
- PSNR
    - Good to look at but because the data given is already collected from MR, it is a reflection of the acquisition
    - All we are doing is further post-processing
    - PSNR pre-determined in acquisition
    - Review this metric once the prototype is ready
- Structure similarity index
    - Many ways to evaluate similarity between structure
    - Other ways to evaluate similarity:
        - DICE similarity: Shared Doc: https://radiopaedia.org/articles/DICE-similarity-coefficient
        - Compare histogram similarity
            - If CT and pCT are true to each other this should be equal
        - Compare visually
            - Can it capture details that CT can normally capture?
    - Simple parts are also important
- Important to have evaluation criterion but we may need to revisit this as the project moves on
    - Some factors might not be included or some factors aren't too important
    - Will likely need to be remodeled
- Spatial resolution
    - Very easy to achieve high-resolution scan with a traditional scanner
    - With MR the final resolution sometimes means that a longer scan will be needed, resolution in MR and CT relates to FOV/sampling points to get spatial resolution
    - Not easy to achieve very high resolution in MR
    - While it is important to try to make the spatial resolution as close to CT as possible, there are many limitations

        - Image resolution has been determined in the acquisition of the given MR
        - Many ways to increase the resolution
            - i.e. We can interpolate fake points to increase resolution (256 x 256 to 512 x 512) although it is not a real image it is fabricated
        - Can request for higher resolution images later once prototype is ready
    - pCT is not meant to replace CT completely
    - When we have prototype we can revisit the evaluation criteria/requirements

Topic #2: Comments about Image Analysis

- When it comes to registration, can consider to downsample for same resolution, ensuring that the two images have the same matrix size
- Do not need the step for CT downsampling for the time being
- Not going to be able to obtain 0.3 mm resolution for MRI, this metric is optimistic
- Tend to look at specifications as satisfied or not, an overall weighted matrix does not guarantee each threshold is achieved
    - Not to place heavy importance on satisfactory metrics
- Utilize the first iteration to revisit the evaluation criteria and reconsider identified metrics
- Value Proposition:
    - Improved resolution to be reconsidered since it is fixed
    - Any type of radiation therapy will have orders of magnitude delivered higher than CT, with regards to dose administered
    - CT scan takes seconds whereas MRI is always minutes longer, not sure if we can talk about reduced times for CT
        - Always have waiting times for MRI and not so much for CT
        - Need to think about use cases:
            - Pediatric application:
                - Patient will be in the scanner anyway
                - Can serve as additional use of scanning sequence without adding time
    - pCT is not going to save time
    - For radiation therapy, yes there will be slightly less radiation exposure but even CT scans do not have that much radiation
    - MR guided therapy can be used to identify tumors and assist in treatment planning
    - 10 different MR scans, if you have to go through radiation therapy the patient does not need an existing scan
    - When planning for surgery or treatment we can layer images and get more information
    - Radiation therapy CT scan is a must right now
        - We want them happening in one place

        - Revisit the value proposition at intervals and evaluate which criteria are being met
- Different aspects
    1) Time and resource savings of not doing multiple scans
    2) MR better soft-tissue contrast
        - Most tumors are soft-tissue contrast
        - Why is CT used? HU estimation is used to get the radiation dose profile and better bone visualization
        - Don't need to worry about superimposing a CT image on the MR to see where the tumor scans
        - Many cancer care centers want to start working on MR-only workflows
            - Such as Cancer Care Manitoba
        - Siemens already has an AI based solution for MR-only workflow which is not working great right now and a UTE based option could work better
        - Already have a sCT workflow which is not great bone-air interface segmentation, especially in regions of the brain

Use case

- Patients who are undergoing MR anyway, pCT gives them a better opportunity to plan radiation therapy
- Cancer centers
- Improved bone/air separation → because of the UTE-MR
- Improved cortical bone → because of the UTE-MR
- MRI and CT need to be registered to one another, by MRI we can delineate tumor very well but in registration process there is an error it is better that we do planning straight from MR however current planning using HU information from CT
- Many planning algorithms are based on using HU to calculate radiation dose
- Treatment planning algorithms are based on CT, so in MRI to sCT algorithms do not work as well due to factors such electron density

Topic #3: Deliverables

- Share the presentation for concept generation with the client before next Thursday
- Shared Documents:
    - DICE Coefficient: https://radiopaedia.org/articles/DICE-similarity-coefficient
    - MRI in Radiation therapy: https://www.magnetomworld.siemens-healthineers.com/hot-topics/mri-in-radiation-therapy
        - QA material which includes the prototype from Dr. Lumeng
        - Publications which include distortion analysis and sCT generation

Topic #4: Concept Generation

- Siemens current process uses something like GAN

- Idea is to use UTE based image to create pCT
- How you get from A to B are all valid approaches
- Client does not want to generate CT image from MR image of a patient using GAN, instead want to use UTE based transform with possible deep learning

Table A9. *Action Items from the Fourth Client Meeting.*

Actionable	***Persons Responsible***	***Deadline***
Concept Generation Presentation	All	Tues. Studio Block (Oct 29)

Client Meeting #5

Date: November 07, 2024

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Gerald (Jerry) Moran, Lumeng Cui, Asieh Tavakol
- *Faculty Supervisor:* NA

Meeting Minutes

Topic #1: Meeting Frequency
- Possibly meeting less
- Best strategy: Biweekly meetings or less frequent
- Capstone team will discuss meeting frequency and get back to Lumeng
- Biweekly meetings, expect to see some progress or actual discussion on the project
- Every Thursday Capstone team can send email providing update on progress of the project

Topic #2: Comments about Presentation
FSD:
- UTE is called sequence acquisition
    - Do not use the term 'sequencing'
- Image registration: Why would we need image registration between inverse scaling and bone-air segmentation?
    - Image registration is more suited for validation to compare pCT to CT
    - Change this in FSD, we can remove this from the automation workflow
    - Do need an image registration technique, but only for assessment/demonstration of the workflow as a form of evaluation
    - Temporarily remove and move into evaluation phase
- Overall diagram is nice, with deep learning strategies and artifact removal mentioned

Deep-Learning Methods:
- If going to explore deep-learning we will need the image registration step
    - Want to make sure MR and CT images are co-registered to train network more easily
    - Probably do not need registration between inverse log and subsequent step
    - Literature review: Have we looked at U-net?
        - U-net is a CNN-based method

        - Used for image segmentation
        - Lumeng will provide some paper on this method: https://www.sciencedirect.com/science/article/pii/S1120179721002714

Evaluation Criteria:

- Change based on the first prototype, might need to do modification afterwards
- Leave the evaluation criteria as it is for now until prototyping

Regulatory Considerations:

- Regarding accuracy of clinical diagnosis
    - In ideal world, we would want prototype to be as clinically accurate as possible
    - This project is R&D, although we want to be accurate, it is not our job to ensure clinical standards are fully met
    - Important for us to treat this as a proof of concept project, making sure it works, then use EC to demonstrate we have good reliability + scores in prototype
    - Try not to focus on clinical accuracy of prototype
    - First get prototype out
    - Patient privacy, make sure data is anonymized and data is handled carefully
    - As R&D we do not need to think about FDA approval, just make things work and then make sure it complies with regulations and laws
    - Not saying accuracy is not important, just not R&D job that these items are met
    - Do not think about these regulations when developing prototype
    - Since we are focusing on post-processing, we are not affecting anyone directly with our work

Topic #3: Deliverables

- Focus on how to extract the bone structures(signal) from images
- Although certain regions may appear dark the signal is still present, with the bone and the background having a small difference
- Intensity values of the image vary, which could be useful in bone-segmentation
    - Try to separate based on values (i.e. background 0, skull ~1.5, soft-tissue~10)
- Histogram-based thresholding is a useful method that should be explored for separating bone from background and soft tissue
- Try using 3D Slicer to do image processing and later explore conversion to code
- Make use of the chicken data provided for image processing in 3D Slicer
- Lot of tutorials online (YouTube) for ImageJ and 3D Slicer to get started with
- Can use third party materials in ImageJ and 3DSlicer for further image processing

Table A10. *Action Items from the Fifth Client Meeting.*

<table>
<tr><th>Actionable</th><th>Persons Responsible</th><th>Deadline</th></tr>
<tr><td>Read Through the Two Papers Sent by Lumeng
https://onlinelibrary.wiley.com/doi/10.1002/mrm.25545
https://jnm.snmjournals.org/content/56/3/417.long</td><td>All</td><td rowspan="2">Tues. Studio Block (Nov 12)</td></tr>
<tr><td>Load Images into 3D Slicer/ImageJ and Try Different Modules to Reproduce Steps in the Paper</td><td>Lynn, Aly Khan</td></tr>
<tr><td>Use Code to Reproduce Results from 3D Slicer/Image J</td><td>Manan, Yuheng, Jackson</td><td>Tues. Studio Block (Nov 19)</td></tr>
</table>

Client Meeting #6

Date: November 21, 2024

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Lumeng Cui, Asieh Tavakol
- *Faculty Supervisor:* Tim Salcudean

Meeting Minutes

Topic #1: Feedback on Presentation

1) Do you guys have a better understanding of the workflow of the project?
    - Yes, going through the papers was very helpful, which allowed us to perform transformations and bias-field correction
    - It is important to see input and output images
2) Why would you need a Gaussian blurring?
    - Usually this just smooths out the image
    - Good thing is we can sometimes use to denoise
    - Downside is we lose a lot of details
    - Do not need to worry about the denoising part in our workflow, there are many methods already existing
    - Depends on what kernel set is being used
    - Relevant for implementation locally, not globally
    - Probably do not need to include in the workflow
3) What is the purpose of normalization?
    - Normalization (0 to 1), done correctly
    - Want to do this first, before inverse-logarithm scaling (Figure #X)
        - Want to keep intensity between 0 and 1 to keep the first part of the -log(image)
        - Want soft tissue to be dark for inverse log transform
        - If we do not control input by normalizing, the inverse log could be changed in the output
    - After loading image, need to do inverse logarithm
    - Image needs to be DICOM format

- Want to create threshold, using histogram after performing a gaussian fitting so we could obtain a 'bone-only' image
    - Can quickly pinpoint threshold after gaussian fitting

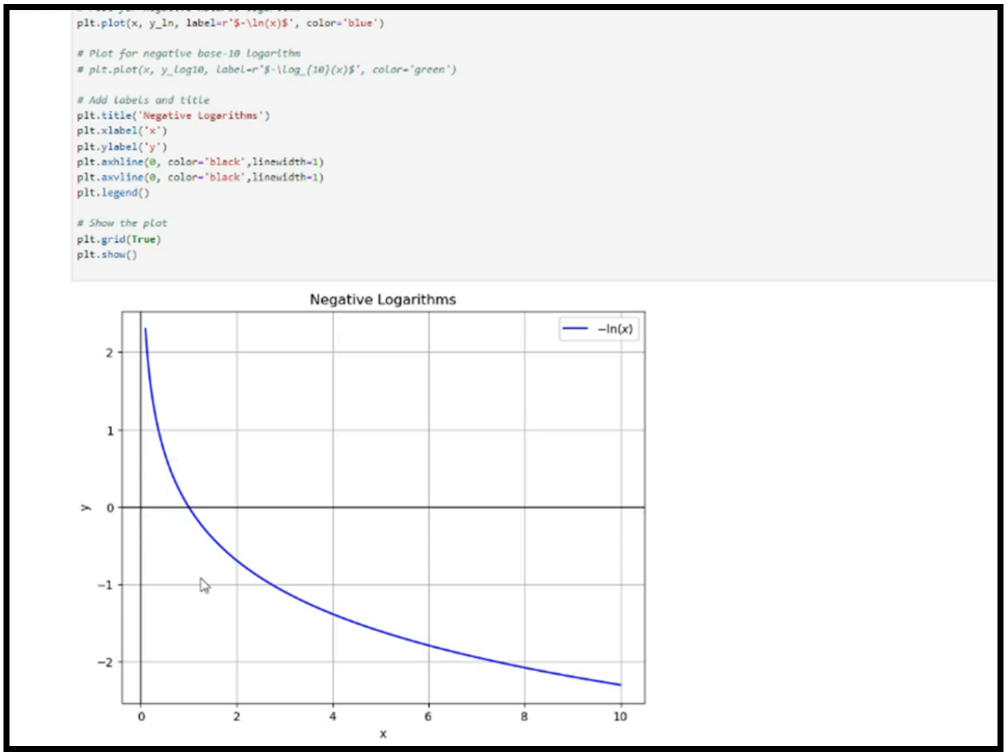

Figure A7. *Graph of Inverse Logarithmic Function.*

- Explore idea of how to implement a bias correction method that creates two narrow peaks within the histogram
- Gaussian fitting, is being applied to histogram to get a nice curve in order to determine the threshold which should be used
- After this we want to do histogram normalization
    - If your workflow works for chicken data and if given MR with human head data will be different, histogram normalization can help us to choose threshold in a standard way
    - For example, threshold will always be between 0.2 and 0.8 for bone

Topic #2: Critical Function Prototype

Image Segmentation

- Setting up threshold can be considered as segmentation process, able to differentiate between soft-tissue and background
- If threshold is chosen correctly should be able to segment out bone-only structure
- Not sure if it is reasonable to come up with deep-learning algorithm for such a short amount of time to the CFP presentation
- Once this is done, we can look into deep learning algorithm to use

Purpose of Deep Learning

- Improve segmentation technique
- Show chicken results, after histogram maybe manually do some thresholding
- First prototype, results will never look perfect but will show some progress
- Suggestion for deep learning, this stage may be too early to demonstrate
- Maybe just show deep learning literature review instead of specific applications

Table A11. *Action Items from the Sixth Client Meeting*

Actionable	***Persons Responsible***	***Deadline***
Perform Transformations in 3D Slicer	Lynn	Monday (Dec 25)
Document the Process for Testing & Verification	Aly Khan	
Implement the Code for Image Background Segmentation	Jackson, Manan	
Describe Key Functions of Prototype and Concept Selection	Yuheng	

***Client Meeting** #7*

<u>Date:</u> November 26, 2024

<u>Attendance:</u>
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Lumeng Cui, Gerry Moran

<u>Questions:</u>
- What is the best way to validate our results?
- Do we have the correct concepts for scoring?
- Does our function structure diagram correctly capture the workflow?

Meeting Minutes

Topic #1: Comments about CFP Presentation
- In general looks good, minor modifications needed
- For the normalization step [0,1]:
  - After performing bias correction we want to normalize data and then do inverse-logarithmic scaling
  - Do not need to rescale back to 255 intensity
    - For example, only resize if we want to export the image to DICOM format
  - Want every input image to be normalized from 0 to 1 regardless of the input
- Breakdown first section into more detailed steps
  - Save intermediate images by rescaling them to 255
  - Can export to 12-bit or 16-bit if more bit is needed
- Assumptions
  - First sentence: Mentions consistent spatial resolution
    - Idea is to work with images of any resolution
    - Want to make sure that when obtaining the image, the scan follows a standardized protocol (specifically UTE sequence)
    - Do not necessarily need consistent spatial resolution, as this would not be possible realistically
    - Without using UTE, bone signal is very small
    - If UTE is used, there will be a bone signal so we want to make sure that this is the case
  - Assumption is that the image must be acquired via UTE
  - Not sure about the second assumption:

        - Want to make sure workflow is robust enough that it is compatible with images from any MRI scanner
        - Instead say, "want to make sure workflow is robust enough that it can work with any scanner, but the scan protocol must be standardized"
            - Want TE and TR to be somewhat consistent
            - Although you are only provided with one dataset, the workflow is meant to be robust
- Limitations:
    - Elaborate on limitations to include future work so that any constraint is worked on or improved upon
    - Reword first sentence as follows: "right now we are only working with a limited number of data but once we have a concrete workflow, we will test the prototype with more datasets"
- With the current workflow (synthetic CT workflow), we want to use deep learning to improve the segmentation technique
- Testing:
    - Compare the bias-corrected and uncorrected image histograms to see if there are any noticeable improvements
    - N4ITK bias-field correction is likely not good enough
    - Might need to look at a different method/module, like the one mentioned in the first paper which used histogram intensity correction
    - After inverse log scaling, we want to make sure there are two narrow peaks
- Better if we show the images where the mask has been applied, not the mask itself
    - Apply the mask to the inverse log rescaled images
    - Also show the CT images for comparison
        - Try best to present CT images with matching orientations

Topic #2: Questions

<u>Do we have the correct FSD?</u>

- In the correct order
- Purpose of deep-learning
    - For the bone-tissue segmentation, we obtain synthetic CT output images
    - Only to make things better, not a mandatory component
- What is meant by artifact removal?
    - Some artifacts can easily be removed, sometimes easier to remove during acquisition
    - Remove this from the FSD as it is very dependent on the acquisition process of the images
- OpenRecon Display
    - Brand name for Siemens, if talking about this to our audience they may not know

        - Swap this name for an ‘On-scanner Display’ instead
            - Not really open-source
            - Need framework or interface to be downloaded for support with MATLAB, or Python
            - On-scanner post-processing is often not possible
            - We want this workflow to be standardized and to be a real-time display for the images
    - Segmentation
        - Compare synthetic output with real CT
        - Need registration to ensure that both images are in the same plane
        - Might not have enough time to implement this yet

<u>What is the best way to validate our results?</u>

- Look at DICE similarity score and structure similarity score (SSIM)
- Extract mask images and compare it between the sCT and the CT
- Same process for extracting the bone mask from the CT as from pCT
- Need registration for this step:
    - Either use automatic registration algorithm at the very beginning while registering MR and CT, or take output and register sCT to CT
    - Use 3D slicer or automatic registration in Python
- Visual inspection is also good
    - Comparing the bone in true CT and pCT
- In the future, introduce more metrics or criteria to have more quantitative comparison
- Want to make sure that there is a fair comparison:
    - Workflow or code needs to be modified to ensure this happens
- Compare histograms as a way to validate which should be visually very similar

<u>Do we have the correct concepts for scoring?</u>

- The concepts are probably good enough
- With GAN or U-Net they are commonly used and there is good amount of literature
- For example with U-Net this is used for segmentation all the time
- You do not know until you know so need to experiment for deep learning:
    - Only way is to train data with different models and see which performs best
- Criteria makes sense for now, however, might need to be revisited
- U-Net, 3D and 2D model
    - For this project, client probably cannot provide an extremely large dataset
    - 2.5D model: 1 3D dataset with each slice modelled in 2D
        - Training data with sagittal, coronal and axial plane makes it 2.5D
    - 2.5D works well and is probably good enough for machine learning

Table A12. *Action Items from the Seventh Client Meeting*

Actionable	***Persons Responsible***	***Deadline***
Complete the CFP Presentation	All	Wednesday (Nov. 27)
Perform Concept Scoring		Monday (Dec 2)

Client Meeting #8

Date: December 03, 2024

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Lumeng Cui, Asieh Tavakol

Questions:
- What are your thoughts on our budget? Do you anticipate any purchases to be made?

Meeting Minutes

Topic #1: Comments about Concept Screening, Scoring and Budget
- Client anticipates no urgent purchases to be made
- Can bring up any requests in the future with Gerry
- Must consider GPU resources for next term
    - Depends significantly on DL model that we decide to pursue
    - Cannot make a conclusive decision on computing resources at present moment
    - Do have individual computers to rely on for now

Topic #2: Presentation from Asieh
- Current workflow for radiotherapy:
    - CT has flat tabletop with external laser since positioning of the patient needs to be kept constant in the scanner during treatment
    - MRI and CT are fused for tumor and normal tissue delineation
    - Perform treatment planning and dose calculation on the CT image
- CT shows tumor and edema clearly but MRI does not
- MRI only workflow is needed since it has better soft tissue contrast without any exposure to ionizing radiation
- MRI cannot be used for dose calculation since intensities are based on proton density and magnetic relaxation of tissues
    - Electron densities are required to compute the ionizing doe
- Electron density phantom is a solid water disk for tissue characterization
- Need sCT from MRI data to inform radiation therapy planning for dose calculation

Table A13. *Action Items from the Eighth Client Meeting*

Actionable	***Persons Responsible***	***Deadline***
Finalize Midterm Budget Review	All	Thurs. Studio Block (Dec 5)
Complete DHFs 1-4		

Client Meeting #9

Date: January 16, 2025

Attendance:

- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Lumeng Cui, Gerry Moran

Questions:

- Based on our concept screening, multi-cycle GANs was ranked the highest, followed by ensemble + grad-cam guided UNET. Would you suggest that we begin implementing the deep learning portion with the GANs or do you have any other recommendation?
- Our team is currently looking at open-source models, just to get an idea of the implementation process. Is this a valid approach? Do you have any suggestions or possible considerations that we should be aware of when searching for these models?
  - Our current findings:
    - https://github.com/Labrapuerta/CycleGAN-for-Image-Translation/tree/main Cycle GAN (2024)
    - https://github.com/MatDagommer/mri-to-ct Cycle? GAN (2023)
    - https://github.com/MIC-DKFZ/nnUNet UNET (2025)
    - https://github.com/afiosman/UNet-for-MR-to-MR-image-translation UNET (2023)
    - https://github.com/ChengBinJin/MRI-to-CT-DCNN-TensorFlow DCNN (2020)
- At the start of last term, it was mentioned that we would be provided training/test data. Would it be possible to receive paired human UTE MRI/CT images for our future training (other than the chicken phantom)?
- Additionally, it would be great if the data provided is representative of the human anatomy (skull etc). Would this be feasible?
- Just to confirm, would it be okay to use all of our evaluation criteria when testing out the existing methods? And then decide from there which criterion is the best, as we had talked about earlier?
- Do you think it would be possible that we might require cloud storage solutions down the road? Depending on the size of our images.
- Where would you place the MRI to CT conversion in the workflow with respect to the bone/air/tissue segmentation?

Meeting Minutes

Topic #1: Questions

- Based on our concept screening, multi-cycle GANs was ranked the highest, followed by ensemble + grad-cam guided UNET. Would you suggest that we begin implementing the deep learning portion with the GANs or do you have any other recommendation?
    - Lumeng will talk to colleague to see if dataset can be provided
        - Does not know how much data for 3D models can be given
            - Maybe 2.5D
            - Could trim the data into the sagittal, coronal and transverse planes
    - Begin looking at UNET model
    - Besides deep learning stuff make sure we have a robust pipeline (**PRIORITY) for getting sCT
        - Maybe look at this in parallel with the deep learning portion
    - In theory may be able to replace entire workflow with deep learning
    - Deep learning does not need to be tailored to the current pipeline we have
        - Either find a way to incorporate deep learning into current pipeline or to come up with an entirely separate model from scratch

- When can we expect to receive paired UTE and CT images?
    - Lumeng will talk to colleague this week, may be able to get data by this month
    - Another idea is to try to use current UTE images using existing pipeline to generate sCT and then use the resulting images as a training dataset
    - Some concern over the time it will take to get data
        - Suggestion is to not wait until the midterm period to start setting up pipeline for hyperparameter optimization
    - Require segmentation results with classifier to at least test on some MRI dat
    - In meantime focus on the first task, continue working on pipeline from last year CFP, with hopes to achieve similar quality as the previous papers shared
        - If good quality data is achieved, we can potentially use the images obtained from this workflow as training data

- Our team is currently looking at open-source models, just to get an idea of the implementation process. Is this a valid approach? Do you have any suggestions or possible considerations that we should be aware of when searching for these models?
    - No specific suggestions as of right now, we should explore and look at optimal solutions based on what is available
    - Do not want to put restrictions on this project right now
    - Also need to make sure that licenses are available for open source use
    - Do a literature review to identify similar problems that have been solved by these models

- At the start of the last term, it was mentioned that we would be provided training/test data. Would it be possible to receive paired human UTE MRI/CT images for our future training (other than the chicken phantom)?
    - Lumeng may be able to provide dataset of MR knee images
    - Can continue to work with chicken data in the meantime

- Just to confirm, would it be okay to use all of our evaluation criteria when testing out the existing methods? And then decide from there which criterion is the best, as we had talked about earlier?
    - SSIM and DICE are definitely criteria that are looked at from time to time
    - Not sure for other criteria not sure
    - Can determine which metrics are relevant once testing is done and data is obtained
    - Right now, focus should be on getting pCT that looks almost identical to CT
        - Structure wise, goal should be for pCT to "look real"

- Datasets are difficult to share for the project and it is unlikely to be solicited now
    - Training cannot really be done on a single phantom data
    - Begin looking for open-source dataset online
        - Even if acquisition sequence does not match UTE-MR, it is better than having nothing to test our the model
    - Focus on the robust pipeline and its testing
    - Start to look into alternatives such as readily available open-source databases

- Do you think it would be possible that we might require cloud storage solutions down the road? Depending on the size of our images.
    - Looking at images of 40-50 megabytes
    - Unlikely that cloud storage would need to be purchased

Topic #2: Next Steps

- What constitutes a reasonable next step for optimization?
    - Focus on upping the quality of the previous pipeline done in CFP
    - To evaluate optimization, some CT dataset needs to be provided
        - Might be able to get 3-4 dataset which may be sufficient for evaluation but not for training of deep learning model
    - Clearly show what optimization has been done for bias correction, inverse scaling, image background segmentation
    - For the report, it is important that the first task for the pipeline is wrapped up in a way that makes the client happy since this is the first priority

<u>Action Items:</u>

<table>
<tr><th>Actionable</th><th>Persons Responsible</th><th>Deadline</th></tr>
<tr><td>Bias Correction</td><td>Yuheng</td><td rowspan="3">Thurs. Studio Block (Jan 05)</td></tr>
<tr><td>Inverse Logarithmic Scaling</td><td>Lynn, Aly Khan</td></tr>
<tr><td>Image Segmentation</td><td>Jackson, Manan</td></tr>
</table>

Client Meeting #10

Date: January 23, 2025

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Lumeng Cui, Gerry Moran

Questions:
- Any update on sourcing the data?
- Could we have access to the gold standard CT images for the chicken dataset?
- Some changes were made to the N4ITK bias correction parameters. Are there any other hyperparameters that you think would improve the results?
    - convergence threshold = 10 ^-3
    - number of iterations [50 50 50 50]
    - spline order = 2
- We also tried to work with nifti files instead of PNG, however, the run time for applying the bias correction filter was quite long. Are there any recommendations to make this process faster other than reducing the number of iterations? Would it be sufficient when testing to look at a singular slice or simply continue using the PNG for testing?
- Would you be comfortable with us presenting in front of our fellow capstone students for the next round of presentations and in front of the general public on Design & Innovation Day?

Meeting Minutes

Topic #1: Updates to Workflow

Updates to the bias correction filter:
- Are there any other hyperparameters that you think would improve the results?
    - Share the report after the meeting
    - Image obtained using bias correction filter looks really good, visually looks like it is improved
    - Lumeng will look into different parameters we might want to check
- Important to clarify why exactly/what tests were used to quantify the parameters
- Ideally want to use NIFTI format, not PNG
    - In terms of the processing doesn't really matter whether the format is Nifti or PNG as long as intensity values
    - Nifti also has headers for storing information

- Compile all the changes to the different code sections such as the improved bias correction, before next week's meeting
- Co-register the MRI and CT images to put them in the same space, then we can run the DICE similarity to compare
    - Rigid vs. Non-rigid
    - Can easily do this in 3DSlicer although might be time-consuming
- Looking at CT, we can choose a threshold to extract the bone feature

Topic #2: Tasks for Next Meeting
- Implement the paper's algorithm on top of the current bias correction workflow
- Work on the Gaussian fitting of the histograms
- Automatic thresholding
  **Might be ambitious to get this done in one week
  **Will see how much gets done and then pivot accordingly

<u>Action Items:</u>

Actionable	***Persons Responsible***	***Deadline***
Histogram-Based Bias Correction	Yuheng, Jackson, Manan	Tues. Studio Block (Jan 28)
Gaussian Fitting	Aly Khan	
Automatic Thresholding	Lynn	
Provide Client Access to the Analysis Report Doc.	Aly Khan	Thurs. Studio Block (Jan 23)

Client Meeting #11

Date: January 30, 2025

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Lumeng Cui, Gerry Moran

Meeting Minutes

Topic #1: Updates to Workflow

- Histogram-Based Bias Correction
    - N4ITK (SimpleITK) vs Hyperparameter Optimization / Histogram-based Bias Correction (work in progress)
        - N4ITK histogram on the left looks better
    - Lumeng questions:
        - What method is the left histogram showing
            - Not from N4ITK
            - Mistake made in presentation
            - Result was from the previous week's optimization method which gave better, much sharper peaks especially for the soft-tissue
    - For next time, put the 3 methods we used side-by-side for comparison
        - Label the methods more clearly
    - Do not abandon the N4ITK method, Lumeng thinks that its results are also viable
    - *Question:* Is it ok if we implement both bias correction methods to see which approach is ideal?
        - *Ans:* Can try implementing histogram-based approach on top of hyperparameter-tuned method last week to see if we can get sharper peaks

- Automatic Thresholding
    - Good results obtained
    - Make sure we very carefully choose the parameters when optimizing the thresholds
    - Communicate results to other team members so bias correction can be improved
    - *Question:* Is manual thresholding preferred in some cases for more precise results or should we stick with automatic thresholding since it is more efficient to implement?
        - *Ans:* In the end, we prefer the automatic method but at this stage, manual thresholding is acceptable to get everything working precisely. We can use both methods to see which provides better thresholding and incorporate the bias correction optimizations accordingly

- Would be nice to have an ability to perform manual override if needed

Topic #2: Tasks for Next Meeting

- Document results for why Gaussian fitting is important and how it affects workflow versus simply using a histogram-based approach

Action Items:

<table>
<tr><th>Actionable</th><th>Persons Responsible</th><th>Deadline</th></tr>
<tr><td>Histogram-Based Bias Correction</td><td>Yuheng, Jackson, Manan</td><td rowspan="3">Tues. Studio Block (Feb 04)</td></tr>
<tr><td>Gaussian Fitting</td><td>Aly Khan</td></tr>
<tr><td>Automatic Thresholding</td><td>Lynn</td></tr>
</table>

Client Meeting #12

Date: February 6, 2025

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Jackson Chen
- *Siemens Team:* Lumeng Cui

Meeting Minutes

Topic #1: Updates from last week

Histogram-Based Bias Correction
- Implemented the same method from the papers given by Lumeng
- According to the paper, if we use this method, we should get a better result
    - We want to make the peaks narrower
    - Results from this method are not quite there, what could we optimize to make this work better?
        - Simple ITK performed better, there could be more optimizations we could look into for this method
    - Ask Manan if the paper is sufficient to implement the same method and if we have any questions
- Another idea we had last week was to apply histogram-based bias correction to the optimized N4ITK parameters
- If we think this method is not the way to go we should discuss this so we do not end up spending too much time on this
- Should try to do more work on this before we come up with a conclusion as to whether or not we should implement this

Automatic Thresholding
- Tiny black holes around the bone region
- Even though you an effort was made to select a good threshold, there are some regions labelled as background where artifacts are not supposed to show

Topic #2: Dataset
- For the current pipeline, Lumeng hopes to provide us with an in vivo UTE dataset
    - Maybe ankle or hip images, hopefully can get real life example that we can test with human data for the final presentation
- Datasets should be sent this week
- Still awaiting approval for deep learning, maybe give this another week

        - If there is not approval in another week we will look for some back up data (i.e. open source), which might not be UTE but will at least provide an extra resource for training and testing
        - If there is time and motivation we can try to implement AI methods
    - When we have the dataset we can revisit this topic and look into segmentation networks to generate sCT from MRI
    - If we have enough time we can incorporate this in the final presentation
    - In the end ideally two workflows
        - Traditional workflow (**what is wanted the most and expected)
        - Deep learning method
    - As we are still waiting on data, focus should be on the current workflow

Topic #3: Schedule
- Send Lumeng a message about the timeline for updates for next week

Topic #4: Environmental Impact of the Solution
- Hardware design
- Why are we doing sCT?
    - In the past, if a person needs to go through radiation therapy for cancer diagnosis, they would need to undergo an MRI scan which is the best imaging modality for oncologists
    - After MRI sometimes people need to go through radiation therapy
        - Patient requires CT scan for treatment planning
        - The goal is to use radiation to kill cancer cells
        - CT image is used to delineate the tumor and determine effective dosage
        - Sometimes we also need to use MR images as CT cannot provide good soft tissue contrast
        - Thus, MR and CT are registered together
    - Environmentally, we are reducing the carbon footprint of performing an additional round of imaging
        - Patient would ideally not need to go through CT scan, only MR
        - From hospital perspective, can save power and compute needed

Would pCT ever replace CT?
- Not here yet as pseudo-CT is not the clinical standard
- Reaching this point is will take a lot of time
- Do we really want to replace every scanner? It can also be patient-dependent on whether they are open to radiation or not
- Another reason we want to use MR only, CT will be there for quite a while
- However, in radiation therapy we may want to replace MR due its long scan times

- From ER perspective, people wouldn't want to replace CT with MR as the timing of the imaging modality cannot be replaced
- If we can get software to do this, we can fix a problem without needing a machine

Action Items:

Actionable	***Persons Responsible***	***Deadline***
Histogram-Based Bias Correction	Yuheng, Jackson, Manan	Thurs. Studio Block (Feb 13)
Gaussian Fitting	Aly Khan	
Automatic Thresholding	Lynn	

Client Meeting #13

<u>Date:</u> February 25, 2025

<u>Attendance:</u>
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Jackson Chen, Manan Verma, Yuheng Zhang
- *Siemens Team:* Lumeng Cui, Asieh Tavakol

Meeting Minutes

Topic #1: Feedback on DHF 6

Fault-Tree Analysis
- Software failure part is covered pretty good
- Hardware failure makes sense, if someone asks about this we need to be prepared to explain by giving some specifics or examples that can support some of the statements
- User error suggestion is that there may be some cases
  - On MR scanner there is research sequence and clinical sequence, for clinical sequence they need to be FDA or HealthCanada cleared
  - From time to time, there is some chance that we can identify bugs in clinical sequence, however, this is pretty rare as most have been tested and verified
  - Specify incorrect sequence → should be talking about research sequence as this is where things are likely to go wrong in some cases
- Data misinput → we need to load sequence and set up parameters, because there are humans involved which can result in cases where things can go wrong
  - Maybe specify this in the diagram, technologist may input numbers
  - Maybe do not label it as 'faulty' MR images but when the doctors sees the images they need to be qualified for diagnoses
    - 1) Images with low quality (artifacts-ridden)
    - 2) Images that do not meet clinical standards
  - For current system, it is very rare for images to contain incorrect information

Topic #2: Feedback on Registration
- Not expected to be included in alpha prototype, does not need to be part of pipeline
- More for the validation process, if we want to compare results side-by-side
- Possible inclusion as a standalone to extract evaluation metrics for comparison

Topic #3: Histogram Based Bias Correction
- For histogram-based bias correction how long does it take to process

- N4ITK with hyperparameters seems to do the trick and histogram based bias correction doesn't seem to improve much
- If it doesn't take long to run, maybe leave the histogram-based function in with possibility to either turn it on and off
- Test on other dataset (knee, shoulder) to see if we get different results

Topic #3: Automatic Thresholding - Morphological Closing

- People use dilation and erosion for this as well, not sure if closing is somewhat similar to those methods
- Should see some more difference when changing the kernel size from (5,5) to (7,7)
- Can try samples from other images to see difference when changing the parameters
- Mostly use (3,3) kernel, can also try a larger kernel size to get better results

Action Items:

<table>
<tr><th>Actionable</th><th>Persons Responsible</th><th>Deadline</th></tr>
<tr><td>Histogram-Based Bias Correction</td><td>Yuheng, Jackson, Manan</td><td rowspan="3">Thurs. Studio Block (Feb 13)</td></tr>
<tr><td>Alpha-Prototype Completion Plan & New Data Exploration</td><td>Aly Khan</td></tr>
<tr><td>Automatic Thresholding</td><td>Lynn</td></tr>
</table>

Client Meeting #14

<u>Date:</u> March 04, 2025

<u>Attendance:</u>

- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Jackson Chen, Manan Verma, Yuheng Zhang
- *Siemens Team:* Lumeng Cui, Asieh Tavakol

Meeting Minutes

Topic #1: Comments on Alpha-Design Presentation

- When we transition between different group members, the previous person should give a brief introduction of the upcoming content e.g. ‘Now, __ will introduce __’
- Image comparison along with the histogram can be beneficial to orient the audience
- It would be nice to show inverse logarithmic mage before inverse log scaling, after log scaling, briefly touch upon what the point of this step is
- Sometimes the presentation is more powerful, if you add pictures instead of just talking through
- Focus on what did you do and the outcome
- For lab demo, suggest to have one person an overview for what the lab demo is about
    - This is the first step → result, second step → result etc.
    - Don’t talk about technical details in the beginning and then have three of us take turns to talk about technical details
    - Then break down the big picture, what code did we use to get there, the details might not be interesting to the audience, more important to talk about results first and then the details

- Begin with the aims of the three major components (inverse log, bias correction, and automatic thresholding)
- Then show the results for each individually
- Then do demo and talk in depth for more details

<u>Action Items:</u>

Actionable	***Persons Responsible***	***Deadline***
Alpha-Design Presentation	All	Thurs. Studio Block (Mar 06, Mar 13)
New Data Exploration		
Initiate Deep-Learning Workflow		

Client Meeting #15

Date: March 20, 2025

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Jackson Chen, Manan Verma, Yuheng Zhang
- *Siemens Team:* Lumeng Cui, Asieh Tavakol

Questions:
- Do you have any feedback on our validation plan?
- Any suggestions for presenting our prototype at D&ID?

Meeting Minutes

Topic #1: New Method for Acquiring Images
- Going to provide a new dataset to run through our pipeline for the ankle
- Holes in images are a result of chemical shift artifact
    - Chemical shift artifact: Bone marrow is fact and can create an interface with water. This generates an artifact which is not representative of the anatomy.
- Lumeng will work on providing another knee dataset with matching reference CT that will address chemical shift artifact without requiring closing or dilation afterwards

Topic #2: Feedback on Validation Plan
- Validation plan looks good
- In the end, the group may find that some metric is more appropriate than another
- While presenting the poster live, put images side-by-side with annotations
    - **Note:** Final meeting scheduled for Tuesday, April 1 before D+ID presentation

Topic #3: Reference Mapping
- Great work on the registration technique
- Suggested to look into existing Python modules that could help save time
- Make sure to talk about the registration step during the presentation
- For subtraction of MR or CT sometimes, pay attention to the data type (Nifti or PNG) to ensure that the intensity between images does not change:
    - For example, Dicom will be an integer (12 or 6 bit) if subtraction is performed so it must be converted to float or double before doing so. This is not the case for Nifti but the group must double-check prior to implementation
    - Once data is on the same scale, difference operation with absolute value can be taken to ensure homogenous results

Topic #4: Permission for Design & Innovation Day

- Put this in writing so both parties can have a record:
    - For presentation, send Lumeng an email to obtain his permission
    - Share the content to be posted on the website so Lumeng can decide after consultation with his colleagues
    - First visual might not be able to go on the website since it is taken from a publication. The group needs to make sure that the images are from the public domain before posting any content online
    - This might not be required for the poster provided proper referencing is done
    - Suggested swapping the image for the provided chicken scans
    - In-vivo images may not be appropriate for sharing on the website either
    - Client name and information is fine for inclusion on the website.
    - Not sure whether the design is ‘real-time’ so may want to consider excluding that from the project title
    - Text looks appropriate at first glance
    - Client is more concerned about permission for usage of visuals

Topic #5: Suggestions for Poster Presentation

- Nothing at this point but can look into providing feedback closer to presentation date
- Suggested the group to reach out for any guidance

Action Items:

<table>
<tr><th>Actionable</th><th>Persons Responsible</th><th>Deadline</th></tr>
<tr><td>Design & Innovation Day Deliverables</td><td>Aly Khan</td><td>Sat. (Mar 22)</td></tr>
<tr><td>One-to-One Reference Mapping</td><td>Jackson</td><td rowspan="2">Tues. Studio Block (Mar 25)</td></tr>
<tr><td>Verification & Validation</td><td>Lynn, Manan, Yuheng</td></tr>
</table>

Client Meeting #16.

<u>Date:</u> April 01, 2025

<u>Attendance:</u>
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Jackson Chen, Manan Verma, Yuheng Zhang
- *Siemens Team:* Lumeng Cui, Asieh Tavakol

Meeting Minutes

Topic #1: Client Forms
- Lumeng will be on leave from April 7th:
  - Provide client-handoff form for completion
  - Share GitHub repository for review and TLXScale validation

Topic #2: Downsampling CT
- Register images first before downsampling
- Within 3DSlicer, this is achieved by 'Registration' using 'Linear Transform'
- Lumeng will provide YouTube video for rigid registration
  - Both images will be overlaid on top of each other
  - Can be achieved interactively
  - Exported images will be automatically resampled
- Tutorial: https://www.youtube.com/watch?v=_qbki5QSyD8

Topic #3 Poster
- Try to get rid of the white irregularities in the ankle pseudo CT.
- Visit Wan Wan Chen if there are any issues being faced with the registration

<u>Action Items:</u>

Actionable	***Persons Responsible***	***Deadline***
Share Validation Information with Client	Aly Khan	Wed. (Apr 02)
Complete Registration & Verification Metrics	Lynn, Manan, Jackson, Yuheng	Sun. (Apr 06)
Submit Complete Documentation	All	Fri. (Apr 11)

M2.3.4. Presentations

Please click on this link to view the compilation of all our presentations throughout the year:

Merged Presentations.pdf

M2.4. Electronic Archive

The following GitHub repository serves as an electronic archive for the Capstone Project with Siemens Healthineers, consolidating the software, documentation, and datasets in this course.

Link: https://github.com/Yakuson/MRI-TO-PCT/tree/main

M3. Other Submissions

M3.1. Financial Statements

There were no purchases made for the Capstone Project due to the fully digital scope of our image processing prototype. Hence, no expenses need to be accounted for in this submission.

M3.2. Client Check-Off Form

Please click on the following link to view our signed Client Check-off Form:

Client Check-off Form_LC Signed.docx

M4. Design History File References

[1] National Cancer Institute, "Radiation Therapy To Treat Cancer," National Cancer Institute, Jan. 08, 2019. https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy

[2] "New WHO/IAEA publication provides guidance on radiotherapy equipment to fight cancer," www.who.int, Mar. 05, 2021. https://www.who.int/news/item/05-03-2021-new-who-iaea-publication-provides-guidance-on-radiotherapy-equipment-to-fight-cancer

[3] Cancer Research UK, "Age and Cancer," *Cancer Research UK*, Mar. 04, 2019. https://www.cancerresearchuk.org/about-cancer/causes-of-cancer/age-and-cancer

[4] National Cancer Institute, "Radiation Therapy Side Effects," *National Cancer Institute*, Jan. 11, 2022. https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy/side-effects

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M5. Design History File Appendices

1-A. Comprehensive Stakeholder Analysis

The following groups of individuals and businesses were identified to have a vested interest in the success of the product (*see Table A1*).

Table A1. *Comprehensive List of Identified Stakeholders with Investigation Plan.*

Stakeholder	Justification	Needs & Values	Investigation Plan & Critical Questions
Medical Radiation Technologist	The radiation technologists are responsible for performing diagnostic imaging and radiation therapy procedures. The specialized technique of UTE is adequately suited for cortical bone structures, with echo-times 100-1000 folds shorter than traditional MRI [A1]. A feasible image processing module that can conveniently inter-convert between UTE MRI and CT images would significantly improve the radiology workflow, thereby alleviating the workload of these individuals.	Timeliness of Procedures	What is the biggest problem encountered by medical radiation technologists while performing their daily duties? How can the proposed solution sufficiently address this issue?
Radiologist	The radiologist is responsible for analyzing the images obtained through the diagnostic procedure and would be the primary stakeholder of the project. Currently, it is evident that conventional MRI has reduced contrast for cortical bones due to a lack of 'free water', which significantly decreases image quality [A2]. This compounds the problem for radiologists by making it difficult for them to obtain an accurate visualization, and, thus diagnosis, of the underlying disease. The product would be of immense help	Accuracy of Clinical Diagnosis	Why is appropriate contrast relevant for imaging of cortical bone? How does this affect the ability to accurately diagnose cortical bone diseases? What image processing techniques would facilitate improved contrast?

	to this stakeholder, by facilitating them to provide quality patient care with improved clinical outcomes and welfare.		
Government	The automatic image processing prototype must abide by government regulations in terms of quality, safety, and patient privacy. Within Canada, this would fall under the Medical Devices Directorate of Health Canada. It is extremely crucial for the commercial and clinical success of the product that it complies with all the regulations outlined under the Food and Drugs Act, as well as the Access to Information and Privacy Office to safeguard patient confidentiality [A3].	Legality & User Safety	What are health and safety considerations that need to be addressed for medical imaging technologies? What are some privacy concerns that the solution needs to consider?
Patients	According to the BC Ministry, around 322,000 MRI exams and over 994,000 CT scans were performed in 2023-2024, which yields an approximate 80% increase from 2016-2017 [A4]. Given the rapid rise in the number of patients over the years, it is critical that medical imaging technologies continue evolving to ensure that suitable quality of care is provided. Having an appropriate image processing infrastructure would allow for improved diagnoses and effective therapies to be administered, which would undoubtedly ameliorate patient quality of life, and productivity.	Timeliness of Procedures, Affordability & Accuracy of Clinical Diagnoses	Which aspects of the diagnostic screening workflow are patients not satisfied with and that can be improved upon?
Waitlisted Patients	According to the Canadian Association of Radiologists' Five-Point Classification System, the maximum patient wait time for imaging tests can	Access to Radiology Screening and Clinical	How do the current wait times for radiology procedures negatively impact patient welfare and

	range anywhere from 24 hours to 60 calendar days [A5]. In 2022, the median wait time for CT and MRI scans respectively, were 5.4 and 10.6 weeks [A6]. Hence, it is quite obvious that the existing demand for radiology screening far exceeds the capacity of the medical care system. Using an enhanced imaging technique like UTE would greatly decrease the time required to capture each individual scan, correspondingly increasing the daily patient throughput. This is a win-win for both the infirm, due to reduced wait times, as well as healthcare providers, who can generate greater revenue from the increase in number of patients.	Wait Times	clinical outcomes?
Siemens Healthcare R&D Team	This stakeholder is our client who is providing direct funding, access to proprietary datasets and technical expertise. The work of Siemens Healthcare's developers and scientists [A7] will also be impacted depending on the scope of the UTE-pCT project and the progress made on the automatic image processing pipeline.	Timeliness of Procedures + Accuracy of Clinical Diagnoses	What accuracy threshold would be appropriate? Is training time a major concern?
Siemens Healthcare Licensors and Distributors	Potential conflicts, including storage of proprietary data on non-company specific servers, could arise and must be adequately dealt with to satisfy this stakeholder. Further, these individuals or legal groups could also be impacted by any concerns related to intellectual property, product quality and use of Siemens Healthcare's assets.	Patient Privacy & Consent	To what extent is this project proprietary, and which aspects of the project should we take extra care to avoid divulging? What steps can we take to ensure confidentiality?

Investors	Investors and shareholders of Siemens Healthcare will have a small interest in whether or not our project will be deployable at scale or help current medical imaging projects develop further. Interest will be localized to potential returns on their investment of resources and time into training and mentoring the team.	Feasibility & Product Marketability	What is the return on investment (ROI) that Siemens Healthcare expects to gain from this project?
Family Members	As potential caretakers and agents of the end-user (patients), family members may have a vested interest in the wait times, efficacy, and affordability of the UTE-pCT prototype. They may be involved in decision-making processes informed by one of the project's diagnostic modules.	Timeliness of Procedures, Affordability & Accuracy of Clinical Diagnoses	Which aspects of the diagnostic screening workflow are family members not satisfied with and that can be improved upon?
Insurance Companies	Insurance companies are stakeholders because they are responsible for covering the costs of medical treatments, products, or services provided to patients. In this case, it would be the diagnostic screening performed by the UTE-pCT image processing system. Their interest lies in ensuring that the project is cost-effective and meets regulatory and quality standards.	Affordability & Adherence to Regulatory Standards	What legal drawbacks should be considered pertaining to automated medical systems such as the image processing prototype?

1-B. Complete List of Alternative Solutions

The following 6 state-of-the-art alternatives were identified, along with their strengths and weaknesses, which would guide the design of our solution (*see Table A2*).

Table A2. *Complete List of Alternative Solutions.*

Solution	Strengths	Weaknesses
Zero Echo Time (ZTE) MRI [A8]	- Allows for efficient capturing of short T_2 bone signals because of its zero nominal echo time + high sampling efficiency - The native proton density (PD) weighting provides excellent contrast between air, bone, and soft tissue - With inverse logarithmic scaling, the ZTE images look very similar to CT images (strong linear correlation) - The scanning is silent and fast, which makes it robust to motion	- To achieve proper bone visualization and segmentation, this method needs bias field correction and inverse logarithmic scaling - Plastic signals from the RF coil are visible in the images - Off-resonance blurring is possible at various tissue interfaces
Hybrid MRI-CT [A9]	- No more need for CT scans, which reduces the radiation that the patients have to go through - Systematic registration errors between MRI and CT are reduced, resulting in improved geometrical accuracy - MRI provides better soft tissue contrast than CT - Combines strengths of MRI and CT - The dose calculation accuracy on MRI was within clinical ranges, which means	- The process of assigning bulk densities manually for all the types of tissues can be time-intensive - MRI is more prone to geometric distortions compared to CT, which may affect dose calculation accuracy - No Electron Density Information for MRI, which may lead to uncertainties in dose calculations - Increased cost due to using both MRI and CT scanners

	it’s more realistic/feasible for radiotherapy	
Synthetic CT using Deep Learning [A10]	- The accuracy is much better than the atlas-based approach with a much lower mean absolute error - After training, the DCNN model can generate synthetic CT images in 9 seconds for each patient - This model involves end-to-end learning of complex relationships, which means it doesn’t require manual segmentation, making the workflow more efficient - This model utilizes transfer learning so that high accuracy is possible even with limited amounts of data	- Takes about 2.5 days to train this model on a high-performance GPU - Needs large volumes of data - This model’s performance relies on the MRI and CT images being aligned properly - Histogram matching/preprocessing is required to overcome scanner variability - Accuracy may be limited since it processes 2D slices instead of 3D volumes due to GPU memory limitations
Synthetic CT using Multi Cycle GAN (Generative Adversarial Network) [A11]	- This model performs much better than cycle GAN with a better MAE and ME - This model requires 100 epochs (140 hrs) for training the model whereas cycle gan requires 150 epochs to converge (150 hrs) - This model makes use of Z net as a generator which improves image accuracy and retains more high-resolution details - Detailed structures of the synthetic CT generated by multi-cycle GAN are retained and are clear	- It requires a long training time of 140 hours for training the model
Pseudo CT using Patch Based Generation [A12, A13]	- This method allows for local morphologic changes by using information-specific volumes in the patch -This method eliminated the need for image registration	- Requires an MRI and CT atlas dictionary for translation - Needs the MRI and CT images to be aligned accurately in the same spatial origin

	- Visual and quantitative analysis depicted a high similarity between CT and pseudo-CT - Had a computation time in GPU of less than 9 mins	- The feature-extracting method resulted in low-resolution pCT images - Large values of MAE were generated due to the bone being underestimated

1-C. Complete Needs Assessment

The following expressed, threshold and latent needs were compiled after thorough primary and secondary research (*see Table A3*).

Table A3. *Complete Needs Statements with Latent Needs Included.*

Key: Expressed Needs (EN), Threshold Needs (TN), Latent Needs (LN)			
ID.	**Description**	**Needs & Values**	**Needs Statement**
1. (EN)	It is incumbent for the image processing prototype to facilitate accurate clinical diagnosis as not doing so would essentially render the design useless. This need goes hand-in-hand with other needs (2, 3, 4, 5) that correspond to enhanced image quality. This can be achieved through implementation of processing techniques that ameliorate parameters such as resolution and contrast while adjusting for noise and artifacts [A14]. It is clear that sufficiently and distinctly characterizing the anatomical components within the image would yield improvements in the validity of clinical outcomes.	Accuracy of Clinical Diagnosis	The prototype enhances geometric fidelity via synthetic CT images, thus improving the quality of diagnosis.
2. (EN)	Distinct segmentation of the boundary between cortical bone and air is a prominent issue that current algorithms are still struggling to successfully implement, with many producing ‘hallucinations’ that do not reflect the actual anatomy [A15]. Moreover, as stated in literature, achieving correct bone-air segmentation is integral for formulation of electron-density and attenuation-correction maps that guide effective dose exposure for radiation therapy [A16]. Hence, it is critical that the design workflow adequately addresses this	Bone-Air Interface Segmentation	The prototype successfully segments the bone-air interface on UTE MR images, addressing limitations of currently implemented algorithms.

	need through integration of valid post-processing techniques, potentially via use of deep learning methods.		
3. (EN)	Image resolution corresponds to the detail of the information captured, which for medical purposes usually entails the anatomy or physiology of the patient [A17]. The client shared that poor resolution is one of the key reasons that led to their most recent synthetic CT AI-product not being widely adopted in the imaging space. Thus, it is essential for the design of the image processing prototype to prioritize achieving good spatial resolution through utilization of noise-reduction techniques.	Image Quality + Resolution	The prototype provides an image with good resolution and minimal artifacts present.
4. (EN)	One of the main issues with the current algorithm implemented for synthetic CT images is poor contrast between bone and soft-tissue. This is particularly problematic as it makes it difficult for radiologists to accurately distinguish between different anatomical structures and to make appropriate diagnoses [A18]. Hence, it is critical that the image processing prototype addresses this limitation adequately through UTE-MR imaging.	Bone-Soft Tissue Interface	The prototype successfully preserves contrast for an accurate bone and soft-tissue interface representation.
5. (EN)	As mentioned earlier, the client explicitly stated their desire for the prototype to manipulate intensity values via conversion from MRI to CT images. Fundamentally, this would be accomplished by two techniques: inverse logarithmic scaling, which enhances image quality by amplifying darker pixels plus compressing brighter pixels, and bias-field correction, which normalizes the image by removing	Intensity Values Adjustment	The prototype correctly transforms the intensity values of MRI scans to those of CT images by using techniques such as inverse logarithmic scaling and bias-field correction.

	unwanted features not conforming to anatomy, called artifacts [A19].		
6. (TN)	As hinted at during our interactions with the client, adhering to regulatory standards while protecting patient privacy is a non-negotiable feature of the design. Although the data provided would be anonymized with no identifying information of the patients themselves, it is evident that this need must be respected at all times. It is imperative that patient data be guarded and secured, with no unintended leaks occurring within the proposed pipeline [A20]. This would be accompanied by thorough research on existing licensing agreements for public, open-source data to ensure that adequate checks are in place before the information is channeled for training of our machine learning component.	Regulatory Compliance	The prototype trains on private and public data as permissible by their license agreement while storing the provided images on a secure, PHIPA-compliant service.
7. (LN)	As mentioned previously, the fairly novel use of Ultrashort Echo Time (UTE) has significantly reduced the time needed to capture scans of the cortical bone when contrasted with conventional MRI [A1]. Hence, the inclusion of the specialized UTE technique for conversion of MRI to CT images would also yield the added benefit of faster radiology procedures. This could further result in shortened wait-times and consequently, more patients being able to benefit from screening and diagnosis.	Timeliness of Procedures	The prototype reduces the time taken for radiation technologists to obtain the MRI scan and for radiologists to diagnose the pseudo-CT image of cortical bone.
8. (LN)	It was categorically stated during our initial meeting with the client that the product could either be standalone or integrated on the cloud with platforms	Accessibility on Cloud	The prototype securely interfaces with Siemens' proprietary image reconstruction platform on the cloud.

	such as Open Recon, which is Siemens' exclusive software for image processing. While it is serviceable to create an independently operable design, ensuring consolidation with existing digital infrastructure would significantly boost accessibility and the likelihood of the prototype being adopted widely within the commercial medical imaging space.		
9. (LN)	Our primary focus for the image processing prototype would involve working with short, dense tissues such as the cortical bone. These structures are typically difficult to capture via traditional MRI techniques and has become a significant challenge to overcome using simple reconstruction algorithms [A15]. Given the weight of the problem, the client has advised us to consolidate our efforts towards primarily addressing this shortfall. Thus, we would mostly be limiting our attention towards the cortical bone and similar T2 tissues. However, the client has encouraged us to consider other tissues, including longer T1 segments, within the workflow. Consequently, while not critical to the functioning of the working prototype, if time-permitting, different tissue types would be incorporated within the overall design as well.	Performance on Different Tissue Types	The prototype successfully converts UTE MR images of short T2 tissues, including cortical bone, to CT-like images, potentially achieving similar results for longer T1 tissues.
10. (LN)	During our client meetings, it was categorically mentioned that our primary deliverable would be an automatic image processing prototype that generates CT-like images from MR scans through inverse logarithmic scaling and bias field correction. The machine learning aspect is a bonus feature that would be incorporated	Machine Learning Component	The prototype includes advanced machine learning techniques for image post-processing such as deep learning or multi-cycle GANs.

	in the image background segmentation portion of the workflow, time-permitting. Hence, this can be classified as a latent need that would be great if included but is not the primary goal of the design.		

1-D. *Complete Requirements*

The following 6 requirements were curated from the most significant needs along with their associated quantitative parameters (*see Table A4*).

Table A4. *Complete List of Requirements with Associated Need ID.*

#	Requirement (Need ID)	Value and Type	Justification
1	Spatial Similarity (ID #1)	Must achieve an average symmetric surface distance (ASSD) of less than 1mm	The geometric fidelity of the generated pseudo CT images from MRI can be evaluated by using ASSD for comparing the geometric distances between features in the pseudo CT and the real CT [A21]. The threshold for the ASSD level MR radiation therapy was researched to be less than 1 mm which is used as the minimum threshold [A22].
2	Bone-Air Interface Segmentation (ID #2)	Must achieve an area under the ROC curve value of at least 0.976	This is the Receiver operating characteristic (ROC) analysis in which intensity thresholds are applied to the segments identified as bone and air for quantifying separating between air and bone [A23]. An area under the curve value of 0.976 was achieved in a study after bias field correction, which can serve as an appropriate minimum requirement for the prototype [A23]. Higher values can be considered as improvements for the prototype.
3	Pseudo CT Resolution (ID #3)	Must achieve a spatial resolution of at least 1 mm [A24]	The upper threshold for the spatial resolution in a study for a CT was identified to be 1 mm [A24]. This metric was used to select a minimum threshold of 1 mm for the spatial resolution for the pseudo CT for our prototype since this would be similar to that of an actual CT [A24].

4	Accurate Intensity Distribution (ID #5)	Must achieve a MAE value of less than 174 for bone, less than 22 for air and less than 159 for soft tissue [A25]	We identified Mean Absolute Error (MAE) as an accurate metric to evaluate accurate intensity transformation from MRI to pseudo CT. This is because MAE errors provide an evaluation of the intensity and the contrast of the image based on the different features in the image [A26]. A study conducted found the MAE values to be in the range depicted on the left which was used as a threshold metric for the MAE values for bone, air and soft tissues.
5	Image Quality + Resolution (ID #3)	Must achieve a Peak Signal to Noise Ratio (PSNR) of at least 20 dB	PSNR is a widely used metric for measuring the fidelity between the original CT image and the reconstructed pCT image. Based on 22+ studies on synthetic CT generation from MRI using deep learning methods, the median PSNR across studies involving different body parts was between 25-30 dB [A27]. However, the deep learning methods used may be too advanced for our initial prototype scope. Since 20 dB was the lowest average value across all 22 studies, it would be an appropriate requirement for our prototype.
6	Image Quality + Resolution (ID #3)	Must achieve a Structure Similarity Index Measurement (SSIM) value of at least 0.6	SSIM is a quality metric that measures how much image structure has been lost in terms of structural information based on our human visual system (sharpness, contrast, and brightness) [A28]. Based on 22+ studies on synthetic CT generation from MRI using deep learning methods, the lowest SSIM value measured was 0.63, for a study on the brain [A27]. Accounting for the lack of deep learning techniques for our initial prototype, a minimum SSIM value requirement of 0.6 would be appropriate.

1-E. Complete List of Evaluation Criteria

The following 5 evaluation criteria were adapted from the requirements, with their corresponding satisfaction curves included as well (*see Table A5*).

Table A5. *Complete List of Evaluation Criteria with Satisfaction Curves.*

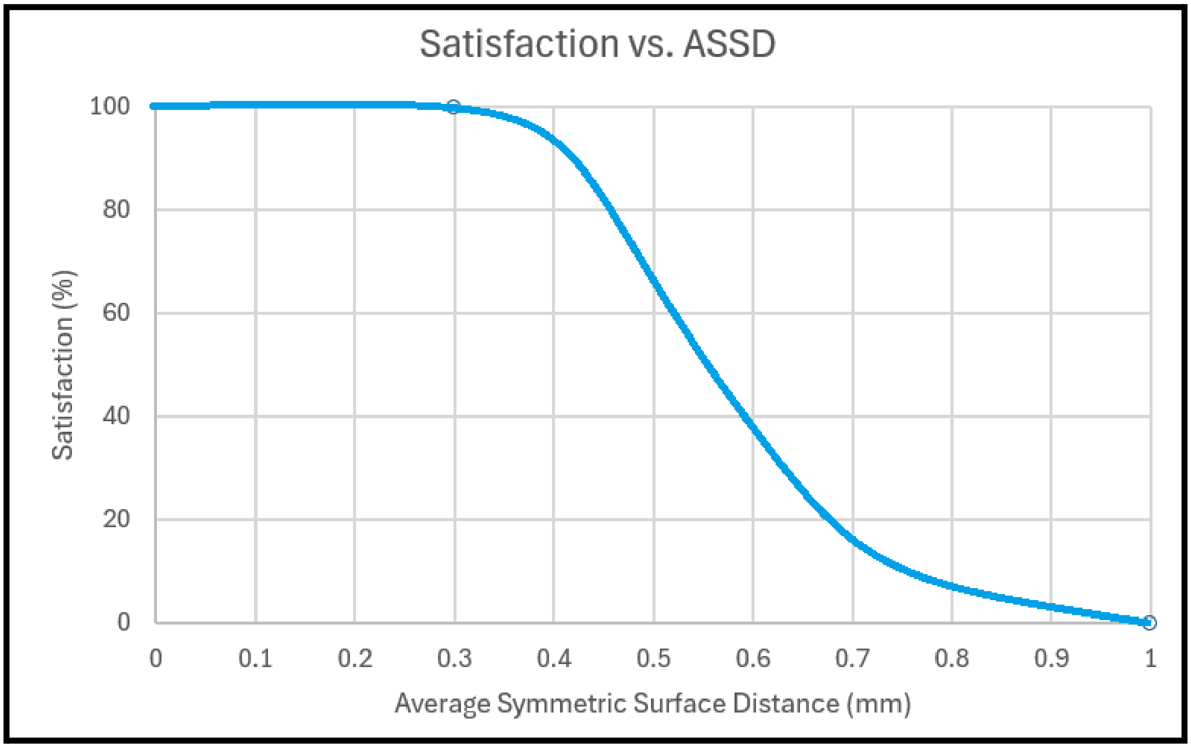
<table>
<tr><th colspan="2">1. Geometric Fidelity</th></tr>
<tr><td>Description: Maintaining geometric fidelity is important for patient safety and accuracy of diagnosis.</td><td>Motivation: This evaluation criteria is motivated by the need for accuracy of clinical diagnosis. (See Section 1.5.1, Need 1)</td></tr>
<tr><td colspan="2">

Figure A1. Satisfaction Curve for Geometric Fidelity.</td></tr>
<tr><td colspan="2">Rationale:
A common method of measuring geometric fidelity is to use the average symmetric surface distance (ASSD). The generally accepted tolerance for geometric fidelity for MR-only radiation therapy should be less than 1 mm [A29][A30]. Anything greater than this value could result in inaccurate information that could harm the patient. Due to this, an ASSD of 1 mm will result in zero satisfaction. If the prototype produces images with anything greater than an ASSD of 1 mm it will not meet requirements, resulting in no added customer satisfaction. As the ASSD number decreases customer satisfaction will increase. The current application used by the client to generate pseudo-CT images was found to have an ASSD of 0.9 mm and 0.8 mm for the pelvic region and brain, respectively [A31]. Ideally, there would be a geometric distortion of 0 mm, however, this is not practically reasonable. Thus, 100% satisfaction will be</td></tr>
</table>

reached at an ASSD value of 0.3 mm. In conducting a literature review the lowest geometric distortion for MRI scanners was found to be 0.3 mm [A29].

Tradeoff:
In increasing the spatial resolution the SNR will decrease [A32][A33]. Lower spatial resolution can increase image distortions, thus decreasing the geometric fidelity [A32].

2. Peak Signal to Noise Ratio (PSNR)

Description: The peak signal-to-noise ratio will be used to measure the quality of the reconstructed pCT image compared to a reference CT image. It is measured in decibels and defined by the equation below [A34].

$$PSNR = 20\,log_{10}\left(\frac{MAX_f}{\sqrt{MSE}}\right)$$

Motivation:
The PSNR of the pCT image will be impacted by the pixel intensity differences, thereby affecting subsequent applications and calculations. This evaluation criteria is motivated by the need for accurate clinical diagnosis, bone-air visualization, image quality, and intensity value adjustment. *(See Section 1.5.1, Needs 1, 2, 3, & 5)*

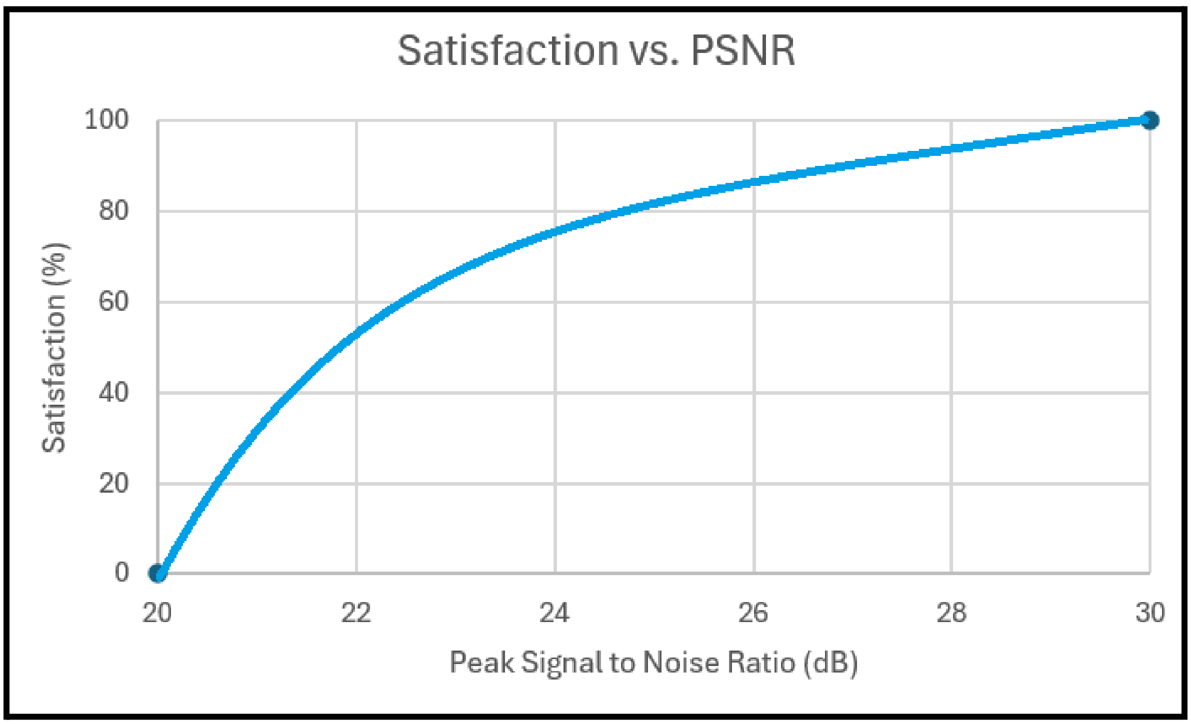


Figure A2. *Satisfaction Curve for Peak Signal-to-Noise Ratio.*

Rationale: Higher PSNR values correspond to better image quality and less noise/distortion in the reconstructed pCT image. Typically, a PSNR of 30 dB or higher is considered good quality [A35], however, a review of relevant literature revealed that in T1, T2, and zero-time MRI-to-pCT conversions, PSNR ranged in the mid-20s [A36]. Therefore, we selected a logarithmic evaluation curve with a 0% satisfaction starting at an x-threshold of 20 dB, to align

with our requirements *(See Section 1.5.2, Requirement 5).* As a PSNR of 30 dB is considered good quality, a PSNR of 30 dB will result in a satisfaction of 100%. This upholds the tenet that satisfaction increases with PSNR while capturing that it would be unreasonable to expect substantial improvement compared to the current state-of-the-art methods.
Tradeoff: PSNR focuses on pixel-wise differences, so this evaluation criteria used in isolation may not align with the subjective image quality observed by a human radiologist.

3. Image Spatial Resolution	
Description: The resolution of the resulting image is important in capturing details allowing for more accurate diagnoses.	**Motivation:** One of the listed needs for the product is that the prototype provides an image with good resolution. *(See Section 1.5.1, Need 3)*

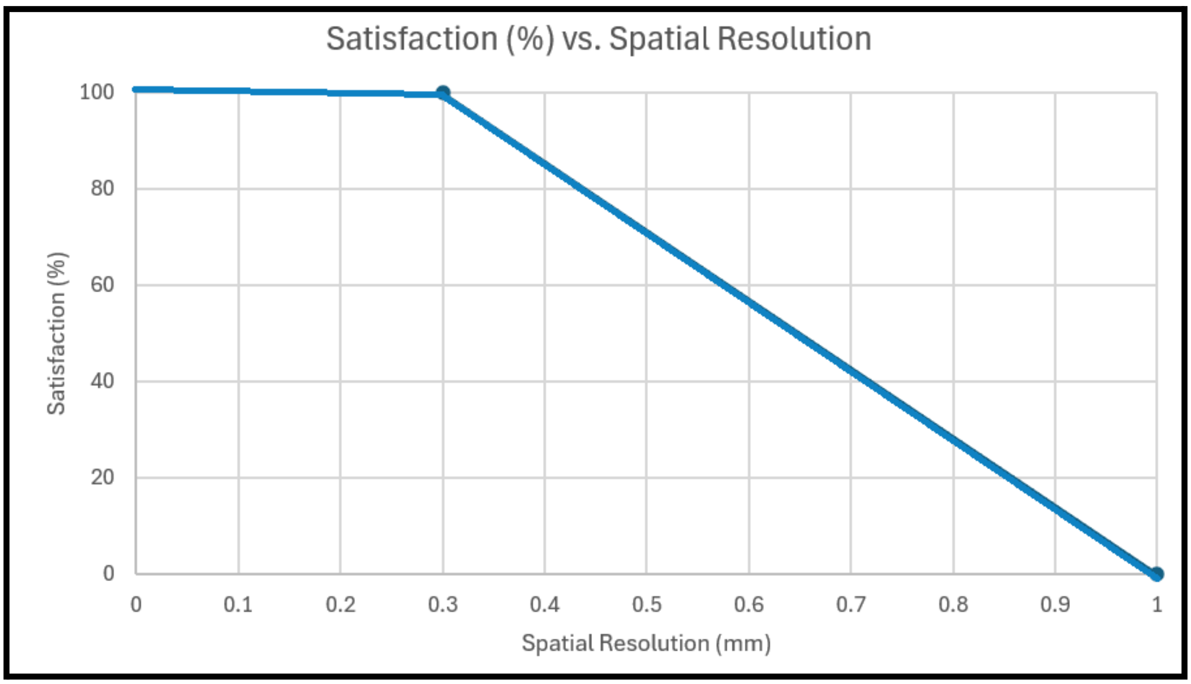


Figure A3. *Satisfaction Curve for Spatial Resolution.*

Rationale:
When discussing the shortfalls of the current application with the client, the product's resolution was brought up as one of the limitations (see Client Meeting #2). The evaluation curve for spatial resolution is linear, as increasing resolution will proportionally increase the customers' satisfaction. Current single-source CT imaging machines from Siemens Healthcare can obtain a spatial resolution of 0.3 mm [A37][A38]. Obtaining 0.3 mm spatial resolution would achieve 100% satisfaction. If the generated pseudo-CT images were able to attain a resolution equal to or better than a standard CT image this would outmatch the resolution of current models. In a study that imaged lungs with UTE MRI to generate pseudo CT a millimetric spatial resolution was obtained [A39]. The particular study used the Magnetom

Skyra and Magnetom Aera from Siemens Healthcare to obtain the MR images.
Tradeoff: In increasing the spatial resolution there could be a decrease in temporal resolution.

4. Structure Similarity Index Measurement (SSIM)

Description: The structural similarity index measurement is a quantitative evaluation metric designed to mimic the human visual system, focusing on luminance, contrast, and texture. It is defined by the following equation [A40].

$$S(x,y) = S_1(x,y)\, S_2(x,y) = \left[\frac{2\bar{x}\bar{y} + \epsilon_1}{\bar{x}^2 + \bar{y}^2 + \epsilon_1}\right] \left[\frac{2s_{xy} + \epsilon_2}{s_x^2 + s_y^2 + \epsilon_2}\right]$$

Motivation: The listed needs for our solution include accuracy of clinical diagnosis, performance on different tissues, bone-air interface segmentation, and image quality (*See Section 1.5.1, Needs 1,2,3, & 9*). The SSIM of the generated pCT image compared to a reference is a good indicator of conversion performance, including interface segmentation and accurate structural representation, which are both important for clinical diagnosis.

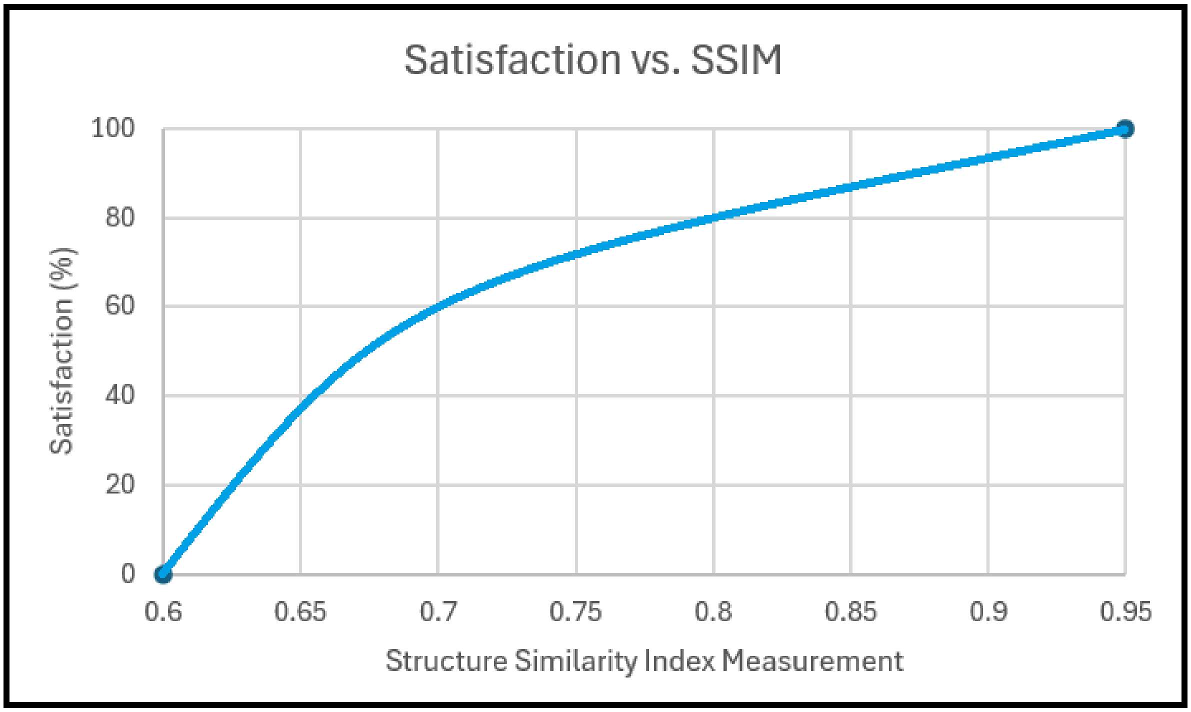


Figure A4. *Satisfaction Curve for Structure Similarity Index.*

Rationale: SSIM values fall between -1.0 and 1.0, with higher values corresponding to higher similarity in brightness, contrast, and texture in the generated pCT image and reference CT image. The range of 0.9 to 1.0 is typically considered ideal for medical applications, however, one literature review looking at the conversion of MRI to pCT yielded an average SSIM of 0.75 to 0.9 with a global minimum of 0.63 [A36]. Thus, we set 0% satisfaction at an x-threshold of 0.60, to align with our requirements *(See Section 1.5.2, Requirement 6)*. A satisfaction of 100% was set at an x-threshold of 0.95 SSIM, as the ideal range for medical application ranges from 0.9 to 1.0 [A36]. A logistical curve was selected to represent this relationship to encapsulate the satisfaction region between 0.70 to 0.95 SSIM.

Tradeoff: Optimising for higher SSIM may result in prohibitively high computational resources or multi-stage processing pipelines being needed.

5. CT Number Accuracy	
Description: Intensity value assignment for the pseudo-CT image.	**Motivation:** This evaluation criteria is motivated by the need which states that the prototype accurately transforms the intensity values of UTE-MRI to those of CT. *(See Section 1.5.1, Need 5).* This criterion is especially important in MR-only radiation therapy to ensure the patient does not receive unnecessary ionizing radiation.

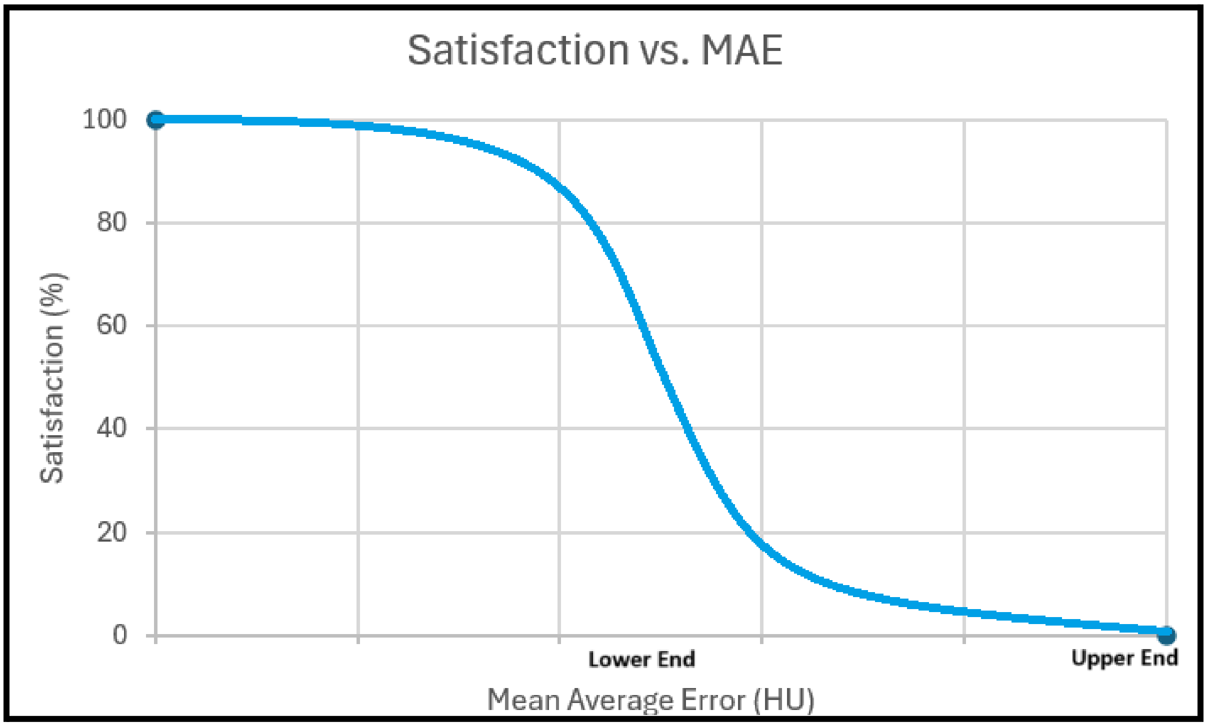


Figure A5. *Satisfaction Curve for CT Number Accuracy.*

Rationale:
As the mean average error (MAE) can differ depending on the structure being imaged the evaluation curve has been generalized to be used depending on the structure or segment. As current solutions for generating pCT from MR images focus on imaging the brain, head and neck, pelvis, and prostate regions we decided to state the typical MAE values for these structures [A41]. Zero satisfaction will be achieved if the listed requirements are not met (*see Section 1.5.2, Requirement 4*). The satisfaction percentage will then slowly increase as the MAE begins decreasing from its' upper range value. Theoretically, a MAE value of zero would achieve 100% satisfaction, however, obtaining a value of zero would be very difficult. Due to this, an S-curve was chosen to reflect the satisfaction percentages. The inflection point

of the S-curve will occur at the lower end of the MAE ranges listed in relevant literature (see below). Anything greater than this value will dramatically increase the satisfaction percentage. For example, for the pelvis, a MAE of anything greater than 65 HU would generate 0% satisfaction with the inflection point at 27 HU. Below are listed MAE for certain structures [A36]: ● Pelvis: **27 - 65 HU** ● Brain: **44 - 129 HU** ● Head & neck: **65 - 131 HU** Below are listed MAE for different segments [A42]: ● Bone: **145 - 203 HU** ● Air: **137 - 181 HU** ● Soft tissue: **19 - 25 HU**
Tradeoff: A potential tradeoff for decreasing the MAE for pseudo-CT could be increased computational times due to higher complexity algorithms.

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1-G. Client Meeting #1.

Summary:
Siemens Healthineers Canada is a subsidiary of Siemens AG, a global technology company with products and services in various markets. Siemens Healthineers Canada's main focus is to deliver innovative solutions to healthcare providers, ranging from medical imaging to laboratory diagnostics. The primary client for this project is Dr. Lumeng Cui, an MR collaboration scientist working for Siemens Healthineers Canada.

The project provided by the client aims to create an automated image processing software to produce pseudo-computed tomography (pCT) from Ultrashort Echo Time (UTE) Magnetic-Resonance (MR) images. Radiation Therapy (RT) for cancer patients requires imaging to aid in the development of a treatment plan to target the malignant tissue effectively. While CT images are commonly used in RT, over the past few years, there has been research in assessing the potential of MRI to achieve improved clinical outcomes. MRI has superior soft-tissue contrast which can help improve localization accuracy. However, MRI has limitations in imaging the cortical bone. One technique aimed at overcoming this challenge is UTE.

Producing pCT from UTE-MR images could help give healthcare providers with adequate alternatives to current, standard imaging protocols for RT treatment plans.

Questions:

- Would you be comfortable with us presenting in front of our fellow capstone students or the general public? (To what extent is this project proprietary, and which aspects of the project should we take extra care to avoid divulging?)
- What tasks would be appropriate to use AI tools for and are there any pitfalls/limitations we should be aware of?
- What are some regulatory obstacles that need to be considered for design of our solution?
- What is the biggest problem encountered by medical radiation technologists and/or radiologists while using MRI for cortical bone imaging?
- What post-processing techniques would facilitate improved image contrast?
- What are some softwares or technologies that would be useful for the project?

Date: Sept. 26, 2024

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Gerald (Jerry) Moran, Lumeng Cui
- *Faculty Supervisor:* Tim Salcudean

Meeting Agenda:
- AI Approval Form - Deadline Friday, September 27th
- NDA
- Access to Existing Literature & Datasets
- Access to Computing Infrastructure
- Alternative Solutions
- Meeting Frequency
- Timeline for Major Deliverables

Meeting Minutes

Topic 1: Introductions of Both Teams
- Capstone team
- Siemens team:
  - Jerry Moran
    - Head of research for Siemens Canada, MRI branching out into CT/PET
  - Lumeng Cui
    - MR Siemens collaborative scientist, supporting St.Paul's Hospital
    - UTE, image processing, and spectroscopy
    - Background in biomedical engineering, master in elastography from University of Saskatchewan
    - Globally responsible for spectroscopy
    - Supports customers in Canada and abroad
- Faculty supervisor
- Note: Stephan Sommer, MR scientist will join subsequent meetings

Topic 2 : Project Overview & Background
- Project goal:
  - Design automatic image processing prototype using UTE to generate sCT
- MR provides superior soft tissue contrast and is mainly used for tumor detection, therapy, and disease diagnosis

- CT better bone visualization modality and provides dose information for radiation therapy
- CT carries radiation, making MR safer
- When trying to collect MR images, some tissues have a short T2 signal that will decay before it can be recorded
- Conventional MR has drawbacks where certain regions such as cortical bone, tendon or meniscus show up as dark areas
- Advantages and disadvantages of both MR & CT - would be good to combine their strengths together
- Bone-air visualization is the tricky part, cannot separate them in MR
- UTE MRI can directly image the bone without any intensity conversion, eliminating the bone-air separation issue
- UTE MRI images can be converted into CT-like images

Topic 3: Project Design

- Task 1: Design an automatic image processing program with the steps:
    - Bias correction (correct signal inhomogeneity)
    - Inverse logarithmic rescaling for enhancing bone contrast
    - Image background segmentation (Retain bone and soft tissue contrast and remove background air)

  Note: For Task 1, design an easy workflow without involving AI or deep learning.

- Task 2: (Time Permitting - Bonus)
    - Use deep learning
    - UTE MR images to train the network and then be provided with testing dataset for generating CT-like images
    - Datasets depend on the progress of the project for training of the network

Topic 4: Expectations

- Deliverable #1
    - Main deliverable: Task 1 is the main deliverable that is expected (Conventional Workflow)

- Deliverable #2
    - Depends on team motivation as well as progress made

- Do not share given data with others

- Development Tools

- Not limited to particular tools
- Suggestions:
    - Python, Github, Jupyter Notebook, ImageJ, 3Dslicer, Microdicom

- Literature
    - Can provide it but the team is expected to do their research
    - Encouraged to seek open-source solutions to address issues

- Meeting Frequency
    - Bi-weekly meeting with Dr. Lumeng Cui for 30 minutes for updates & questions
    - Bi-monthly meeting with bigger Siemens team

- Other
    - Must document the process for meetings, solutions, issues, questions, and action items for each team member
        - Eg: Can use tools like OneNote or Google Doc
    - For additional costs (i.e. poster print) and publications, let Jerry know in advance and can go over it later

- Future Possibilities
    - Siemens decided to go with an AI-based sCT product but the UTE sCT can potentially outperform current technologies with room to improve
    - Faster, easier workflow
    - What is meant by workflow?
        - One automatic program/prototype could be stand-alone or sit on an online interface like Open Recon
            - Ex. if given UTE images program can be run and results will be given
        - Input: UTE images
        - Output: Set of images that look like CT and can be imported into radiation workflow

Topic 5: Upcoming Deliverables

- Before next meeting on Thursday Oct. 3, 2024:
    - Share literature findings
        - See if open source image data sets can be found online
    - Decision on development tools selected and status of setup and configuration of computers
    - Ideas on the design of the prototype (As specific as possible)
    - Breakdown of the project and its timeline for each part

- Resources from client:
  - Can provide UTE images for task #1, CT images only needed for task #2
    - Set of images with both MRI and CT
      - Ensure we can examine them
      - Will be given ASAP
      - Know how to work with Dicom
    - Separate different tasks and discuss findings within the team
    - Faculty supervisor may be able to get CT scans for team to use
  - Slide deck presented during meeting will be shared with references to get started on literature review
  - Shared links:
    - https://www.siemens-healthineers.com/magnetic-resonance-imaging/clinical-specialities/synthetic-ct
    - https://www.nature.com/articles/s41598-024-59014-6

Topic 6: Questions from Students

- AI Approval
  - No uploading images
  - No code generated from AI (Allowed for minor assistance)
  - Open-source package is fine but make sure that it is annotated in the code
  - Segment out section of the code generated by AI with adequate documentation as well

- NDA:
  - Waiting for the paperwork to come back from UBC so that it can be signed

- Computing Resources:
  - Personal laptops will be fine
  - Computing infrastructure is not needed as datasets are not that big

Table A6. *Action Items from the First Client Meeting.*

<table>
<tr><th>Actionable</th><th>Persons Responsible</th><th>Deadline</th></tr>
<tr><td>Progress Slides for Next Client Meeting</td><td rowspan="3">All</td><td rowspan="5">Tues. Studio Block (Oct. 1)</td></tr>
<tr><td>Decide on Computational Tools Required for Project</td></tr>
<tr><td>Draft Ideas for Prototype Design</td></tr>
<tr><td>Expand on Literature Findings (Open Source Images and Tools, State-of-the-Art Modalities, etc.)</td><td>Manan, Yuheng</td></tr>
<tr><td>Download and Look into Medical Image Viewers</td><td>Lynn</td></tr>
</table>

Generate Gantt Chart and Timeline	Aly Khan, Jackson	

1-H. Client Meeting #2

Date: October 3, 2024

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Gerald (Jerry) Moran, Lumeng Cui, Stephan Sommer, Asieh Tavakol, Niranjan Venugopal
- *Faculty Supervisor:* NA

Meeting Agenda:
- Presentation by Capstone Team:
  - Literature Findings
  - Project Timeline
  - Questions for Client

Meeting Minutes

Topic 1: Introductions

Asieh Tavakol
- Cancer Care Manitoba
- Using flexible UTE sequence for synthetic CT generation
- PhD student at the University of Manitoba
- Works as a medical physicist in radiation therapy

Stefan Sommer
- Focusing on UTE sequence and reconstruction
- Works together with Lumeng at Siemens, based in Switzerland
- Tried to do image translation from MR to CT

Niranjan Venugopal
- Medical physicist at the University of Manitoba
- Worked on developing novel techniques
- Using UTE information for developing sCT with applications in radiation oncology

Topic 2: Presentation Feedback
- ZTE is essentially the same thing as UTE, defines the center of timing so that there can be zero echo time **(different nomenclature)
- Deep learning and GAN are two very different models

        - Lots of data
        - Train in 2D or 3D
- Pre processing focused on bias correction and inverse logarithmic scaling (Gets an easy CT-like image)
- Might not have UTE MRI on open image sources
- Identify what is working well or not and what deep learning could help with
- Image segmentation should focus on bone/air separation (Can use histograms for thresholding) and segmenting foreground from background (Could be the most important or challenging aspect)
- Need: Identify where object is after inverse contrast and find proper boundaries
- Use phase imaging of UTE
- Project is not developed in three parts equally
    - Some parts will be more challenging or easier (i.e. image rescaling can be quite easy)

Topic 3: Questions for the Client

- <u>What do you recommend we use the budget on?</u>
    - Access to GPUs for the deep learning aspect
        - Cloud credits
    - If the budget exceeds the limit, it can be approved by the Siemens team

- <u>What are some regulatory obstacles?</u>
    - If an algorithm is trained on public data, the license agreement of the public data should be checked to see if it can be used in commercial settings

- <u>Is there a particular tissue we should be focusing on?</u>
    - The given data will be mainly short T2 tissues (i.e. cortical bone) imaged using UTE
    - Once it is trained we can look into other tissues and retrain the model
    - Asieh has a slide deck highlighting the issues - which may be presented in the next client meeting
    - One of the main problems is that current sCT doesn't do well in capturing bone-soft tissue interfaces and bone-air interfaces
        - Some algorithms produced "hallucinations" (artifacts)
        - The current algorithm is trained by specific MR techniques (ex. T1 weighted) for clinical applications
    - UTE technique can create contrast between the bone and air
        - For brain, this can be an issue due to air space in the nose

- What pre-processing and post-processing techniques should we look into?
    - Bias field correction can help with intensity for pre-processing of images
    - Open to try new processing techniques to improve workflow
        - I.e. come up with our own bias field correction
    - Important to be generalized for many cases
        - Ex. if healthy images are only used to train it can create bias when an unhealthy image is brought on
        - Ex. Had to remove parts of a skull for brain imaging and the model added the skull back as an example so segmentation of the pathology is important
    - In UTE there is some physics differentiating between bone and air

- Siemens already has a sCT AI-based product, what are the shortfalls?
    - Shortfalls:
        - Has been trained on conventional MR images, which cannot differentiate bone and air
        - Not best in terms of resolution (good resolution can go down to 0.3mm)
    - Advantages:
        - Can provide HU units

    - Main Goal is to create a CT-like image with very high contrast between bone and the rest of the tissue and also bone and air (Get as close as possible and don't care about absolute values)
    - First goal is to try to create CT-like image from MR, if there is more time look into creation of sCT which requires the application of HU

- In terms of our approval form is there anything you could think of that would be beneficial for us to add?
    - Gantt chart could also be added into this

Topic 4: Questions from Clients
- Could we record the client meeting sessions?
    - Yes. We can record the client meeting sessions.

Topic 5: Final Remarks from Client
- UTE/ZTE/Petra are all similar but there are some minor differences
    - Don’t need to understand the physics behind
- Ni.gzz files will be given for the images

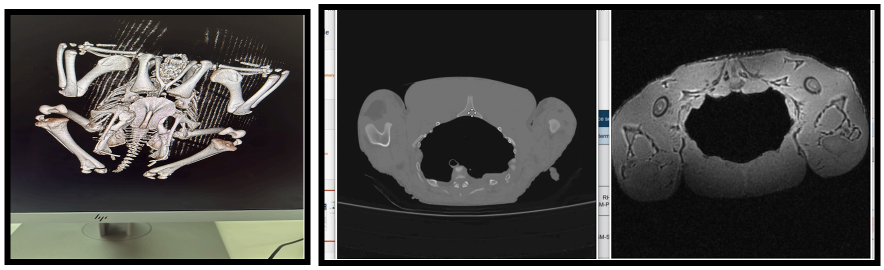

Figure A6. *CT Images of a Chicken Skull.*

Topic 6: Upcoming Deliverables

- Work on a dedicated budget, what is the best options
    - Buy GPU or Cloud Credit
    - If urgent: give a couple weeks heads up to Gerry
- Share feedback/questions on things noticed on the images provided
- Add to meeting minutes what deliverables will be done / presented by next meeting

Table A7. *Action Items from the Second Client Meeting.*

<table>
<tr><th>Actionable</th><th>Persons Responsible</th><th>Deadline</th></tr>
<tr><td>Explore Provided Dataset</td><td rowspan="3">All</td><td rowspan="4">Tues. Studio Block (Oct 08)</td></tr>
<tr><td>Questions for Client</td></tr>
<tr><td>Download Development Tools</td></tr>
<tr><td>Budget and Computational Resources (GPU, Cloud)</td><td>Yuheng, Jackson</td></tr>
</table>

2-A. Client Meeting #3

Date: October 10, 2024

Attendance:

- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Gerald (Jerry) Moran, Lumeng Cui, Stephan Sommer, Asieh Tavakol,
- *Faculty Supervisor:* Tim Salcudean

Questions for the Client:

- What post-processing techniques were added to the corrected image?
- Are there any artifacts (features that do not correspond to the anatomy) present in the image?

Meeting Minutes

Topic 1: Updates for Client

- Our team has been working on getting DHF 1 completed for tomorrow
    - Stakeholder analysis, value proposition, alternative solution
    - Make presentation of DHF 1 progress for next meeting

Topic Questions for the Client

- What post-processing techniques were added to the corrected image given?
    - When UTE images are collected there is a lot of body fat inside the tissue which can create chemical shift artifact, in regular MR this can be fixed
    - UTE uses non-cartesian acquisition which can cause issues with the images
    - Suppress the fat signal and only collect the muscle and other tissues, if this is not corrected it can blur the image creating an off-resonance artifact
    - Given both, suggest using the uncorrected one for prototype
    - Post-processing in corrected image is an ‘in-house’ technique
    - Lumeng will try to find an example of the fat artifact and share
    - Techniques can be implemented in the acquisition

Topic 2: Questions from Clients

- Any issues regarding using Dicom or nifty?
    - Decided to go with 3D Slicer

- What is meant by smoothness?
    - Edges are defined better → Call this sharp instead of smooth

    - CT can provide more resolution but we need to be aware of the contrast
    - 'Smooth' has different meaning in imaging, we are looking for the sharpness hoping that the image can provide a lot of detail and diagnostic information
    - Graininess corresponds to signal-to-noise ratio (SNR)

- What is registration?
    - When MR and CT are collected they are taken separately, although sometimes you want to match orientation and position to be as close as possible
        - In reality, this is not always possible
    - Image registration is used to overcome this
    - Look for a registration algorithm
        - Allow them to have same orientation and same position
        - This can help to evaluate the workflow
        - Some examples, many more to look at:
            - Rigid
                - Simple technique
                - Doesn't matter which one you choose as template or moving image
            - Non-rigid
                - If MR is smaller than CT we can figure out how to scale
            - Elastic registration
                - More complex
                - Deform the MR image in certain way and get it to match up with the CT
    - 3D Slicer includes some registration module
    - There might even be methods that don't require image registration
    - In BMEG 420 course (Medical Imaging) there is a basic introduction to registration and segmentation
        - Look at this for background knowledge
        - Learn how to subsample an image
            - Need to look at CT and bring it down to the same resolution, comparison is difficult when resolution is different
            - Rigid registration in slicer, routines available to do that
    - Do not start with massive non-rigid problem, could be complex
        - Begin with rigid registration
        - Qualitative evaluations of contrast with CT exist as mentioned in the papers provided
        - Robotics and introduction to computer vision (vision and control) textbook available (Robotics, Vision and Control: Fundamental Algorithms in MATLAB/Python - Peter Corke)

            - Examples in MATLAB and Python
            - 2 chapters corresponding to segmentation, image processing, registration etc.
        - Goal of the process is not to develop a good registration method
        - Trying existing methods will be sufficient
    - Do not spend too much time focusing on registration, find what is good enough
    - Certain steps are pretty standard/conventional
    - Look at histograms and see how values are distributed
    - While 3D Slicer can be used, it is important to go over basic image analysis to get a good understanding
    - Have a look at ImageJ, very fast and can directly load images
        - Lumeng has a lot of personal experience using it
        - Look at histogram and do simple processing like inverting contrast
            - i.e. Histogram equalization
        - Doesn't really matter which imaging tool, simply suggestions

Topic 3: Presentation from Asieh

- Challenges in AI based sCT for radiotherapy
    - sCT provides better soft-tissue visualization, eliminates registration uncertainties, reduces costs, and minimizes unnecessary radiation exposure
    - Technical issues:
        - MRI limitation: Has difficulty in separating bone air interfaces especially in sinus regions, causes mri signal to vary and makes it hard to distinguish.
        - Data mismatch: Differences in mri scanner models can lead to inconsistencies and not produce accurate results
        - Lack of standardization: no established QA protocols in hospitals which can result in inconsistencies
        - Data requirements: AI models require large diverse datasets, how we are acquiring the data is important + AI models need to perform consistently across all patient types and scenarios.
            - Ex. A model trained on the brain will have issues when implemented in a pediatric scenario.
        - Bone clarity & Mislabeling: Regions near air cavity, such as sinuses and bones, may not be clear and there may be tissue mislabeling
            - Ex. If soft tissue are near bone they are incorrectly labeled as bone
        - Implant interface: metal implants can lead to artifacts and inaccuracies in dosage calculation
            - Ex. metal implant in jaw could create "bone like structure"
    - The clarity of bone features may be degraded
    - Bony structures near air cavities are less detailed in sCT

- DSC and MAE are mentioned
- A, B, C on the last slide are different algorithms for generating sCT
    - A is better according to metrics
    - Sometimes when there are large air spaces, sCT might not perform as well
    - A only has been tried on pelvis and brain
    - A,B,C are publicly available data
- Presentation will be shared

Topic 4: Upcoming Deliverables

- Go over rigid and non-rigid transformations, identifying which is better suited for the task
    - What methods are available and what did we miss today?
    - What aspect can help with these transformations?
    - Use the BMEG 420 textbook to read up on registration and segmentation (Fundamentals of Medical Imaging - Paul Seutens)
        - Take a look at Gaussian filter (how to visualize air between images)
    - Learn how to subsample an image and bring the resolution of a CT down to that of a MRI
    - Use rigid registration in 3D Slicer for this
- Explore the registration, segmentation and module finder features of 3D Slicer for automatic pipelines
- Explore ImageJ
- Try manipulating the chicken images
- Create slides for next meeting about what has been done, what will be done and questions for the client

Table A8. *Action Items from the Third Client Meeting.*

Actionable	***Persons Responsible***	***Deadline***
Read and Understand the Basics for Image Manipulations	All	Thurs. Studio Block (Oct 17)
Read Two Chapters of *Robotics, Vision and Control: Fundamental Algorithms in MATLAB/Python* - Peter Corke		
Explore ImageJ Software + Make Image Manipulations on 3D Slicer with Chicken Dataset		
Create a Presentation Outlining Progress and Go Over Listed Actionable Items		

2-B. Client Meeting #4

Date: October 24, 2024

Attendance:

- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Gerald (Jerry) Moran, Lumeng Cui, Asieh Tavakol
- *Faculty Supervisor:* Tim Salcudean

Meeting Minutes

Topic #1: Comments about Presentation

- PSNR
    - Good to look at but because the data given is already collected from MR, it is a reflection of the acquisition
    - All we are doing is further post-processing
    - PSNR pre-determined in acquisition
    - Review this metric once the prototype is ready
- Structure similarity index
    - Many ways to evaluate similarity between structure
    - Other ways to evaluate similarity:
        - DICE similarity: Shared Doc: https://radiopaedia.org/articles/DICE-similarity-coefficient
        - Compare histogram similarity
            - If CT and pCT are true to each other this should be equal
        - Compare visually
            - Can it capture details that CT can normally capture?
    - Simple parts are also important
- Important to have evaluation criterion but we may need to revisit this as the project moves on
    - Some factors might not be included or some factors aren't too important
    - Will likely need to be remodeled
- Spatial resolution
    - Very easy to achieve high-resolution scan with a traditional scanner
    - With MR the final resolution sometimes means that a longer scan will be needed, resolution in MR and CT relates to FOV/sampling points to get spatial resolution
    - Not easy to achieve very high resolution in MR
    - While it is important to try to make the spatial resolution as close to CT as possible, there are many limitations

    - Image resolution has been determined in the acquisition of the given MR
    - Many ways to increase the resolution
        - i.e. We can interpolate fake points to increase resolution (256 x 256 to 512 x 512) although it is not a real image it is fabricated
    - Can request for higher resolution images later once prototype is ready
- pCT is not meant to replace CT completely
- When we have prototype we can revisit the evaluation criteria/requirements

Topic #2: Comments about Image Analysis

- When it comes to registration, can consider to downsample for same resolution, ensuring that the two images have the same matrix size
- Do not need the step for CT downsampling for the time being
- Not going to be able to obtain 0.3 mm resolution for MRI, this metric is optimistic
- Tend to look at specifications as satisfied or not, an overall weighted matrix does not guarantee each threshold is achieved
    - Not to place heavy importance on satisfactory metrics
- Utilize the first iteration to revisit the evaluation criteria and reconsider identified metrics
- Value Proposition:
    - Improved resolution to be reconsidered since it is fixed
    - Any type of radiation therapy will have orders of magnitude delivered higher than CT, with regards to dose administered
    - CT scan takes seconds whereas MRI is always minutes longer, not sure if we can talk about reduced times for CT
        - Always have waiting times for MRI and not so much for CT
        - Need to think about use cases:
            - Pediatric application:
                - Patient will be in the scanner anyway
                - Can serve as additional use of scanning sequence without adding time
    - pCT is not going to save time
    - For radiation therapy, yes there will be slightly less radiation exposure but even CT scans do not have that much radiation
    - MR guided therapy can be used to identify tumors and assist in treatment planning
    - 10 different MR scans, if you have to go through radiation therapy the patient does not need an existing scan
    - When planning for surgery or treatment we can layer images and get more information
    - Radiation therapy CT scan is a must right now
        - We want them happening in one place

        - Revisit the value proposition at intervals and evaluate which criteria are being met
    - Different aspects
        1) Time and resource savings of not doing multiple scans
        2) MR better soft-tissue contrast
            - Most tumors are soft-tissue contrast
            - Why is CT used? HU estimation is used to get the radiation dose profile and better bone visualization
            - Don't need to worry about superimposing a CT image on the MR to see where the tumor scans
            - Many cancer care centers want to start working on MR-only workflows
                - Such as Cancer Care Manitoba
            - Siemens already has an AI based solution for MR-only workflow which is not working great right now and a UTE based option could work better
            - Already have a sCT workflow which is not great bone-air interface segmentation, especially in regions of the brain

Use case

- Patients who are undergoing MR anyway, pCT gives them a better opportunity to plan radiation therapy
- Cancer centers
- Improved bone/air separation → because of the UTE-MR
- Improved cortical bone → because of the UTE-MR
- MRI and CT need to be registered to one another, by MRI we can delineate tumor very well but in registration process there is an error it is better that we do planning straight from MR however current planning using HU information from CT
- Many planning algorithms are based on using HU to calculate radiation dose
- Treatment planning algorithms are based on CT, so in MRI to sCT algorithms do not work as well due to factors such electron density

Topic #3: Deliverables

- Share the presentation for concept generation with the client before next Thursday
- Shared Documents:
    - DICE Coefficient: https://radiopaedia.org/articles/DICE-similarity-coefficient
    - MRI in Radiation therapy: https://www.magnetomworld.siemens-healthineers.com/hot-topics/mri-in-radiation-therapy
        - QA material which includes the prototype from Dr. Lumeng
        - Publications which include distortion analysis and sCT generation

Topic #4: Concept Generation

- Siemens current process uses something like GAN

- Idea is to use UTE based image to create pCT
- How you get from A to B are all valid approaches
- Client does not want to generate CT image from MR image of a patient using GAN, instead want to use UTE based transform with possible deep learning

Table A9. *Action Items from the Fourth Client Meeting.*

Actionable	***Persons Responsible***	***Deadline***
Concept Generation Presentation	All	Tues. Studio Block (Oct 29)

2-C. Client Meeting #5

<u>Date:</u> November 07, 2024

<u>Attendance:</u>
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Gerald (Jerry) Moran, Lumeng Cui, Asieh Tavakol
- *Faculty Supervisor:* NA

Meeting Minutes

Topic #1: Meeting Frequency
- Possibly meeting less
- Best strategy: Biweekly meetings or less frequent
- Capstone team will discuss meeting frequency and get back to Lumeng
- Biweekly meetings, expect to see some progress or actual discussion on the project
- Every Thursday Capstone team can send email providing update on progress of the project

Topic #2: Comments about Presentation

FSD:
- UTE is called sequence acquisition
    - Do not use the term 'sequencing'
- Image registration: Why would we need image registration between inverse scaling and bone-air segmentation?
    - Image registration is more suited for validation to compare pCT to CT
    - Change this in FSD, we can remove this from the automation workflow
    - Do need an image registration technique, but only for assessment/demonstration of the workflow as a form of evaluation
    - Temporarily remove and move into evaluation phase
- Overall diagram is nice, with deep learning strategies and artifact removal mentioned

Deep-Learning Methods:
- If going to explore deep-learning we will need the image registration step
    - Want to make sure MR and CT images are co-registered to train network more easily
    - Probably do not need registration between inverse log and subsequent step
    - Literature review: Have we looked at U-net?
        - U-net is a CNN-based method

        - Used for image segmentation
        - Lumeng will provide some paper on this method: https://www.sciencedirect.com/science/article/pii/S1120179721002714

Evaluation Criteria:

- Change based on the first prototype, might need to do modification afterwards
- Leave the evaluation criteria as it is for now until prototyping

Regulatory Considerations:

- Regarding accuracy of clinical diagnosis
    - In ideal world, we would want prototype to be as clinically accurate as possible
    - This project is R&D, although we want to be accurate, it is not our job to ensure clinical standards are fully met
    - Important for us to treat this as a proof of concept project, making sure it works, then use EC to demonstrate we have good reliability + scores in prototype
    - Try not to focus on clinical accuracy of prototype
    - First get prototype out
    - Patient privacy, make sure data is anonymized and data is handled carefully
    - As R&D we do not need to think about FDA approval, just make things work and then make sure it complies with regulations and laws
    - Not saying accuracy is not important, just not R&D job that these items are met
    - Do not think about these regulations when developing prototype
    - Since we are focusing on post-processing, we are not affecting anyone directly with our work

Topic #3: Deliverables

- Focus on how to extract the bone structures(signal) from images
- Although certain regions may appear dark the signal is still present, with the bone and the background having a small difference
- Intensity values of the image vary, which could be useful in bone-segmentation
    - Try to separate based on values (i.e. background 0, skull ~1.5, soft-tissue~10)
- Histogram-based thresholding is a useful method that should be explored for separating bone from background and soft tissue
- Try using 3D Slicer to do image processing and later explore conversion to code
- Make use of the chicken data provided for image processing in 3D Slicer
- Lot of tutorials online (YouTube) for ImageJ and 3D Slicer to get started with
- Can use third party materials in ImageJ and 3DSlicer for further image processing

Table A10. *Action Items from the Fifth Client Meeting.*

Actionable	***Persons Responsible***	***Deadline***
Read Through the Two Papers Sent by Lumeng https://onlinelibrary.wiley.com/doi/10.1002/mrm.25545 https://jnm.snmjournals.org/content/56/3/417.long	All	Tues. Studio Block (Nov 12)
Load Images into 3D Slicer/ImageJ and Try Different Modules to Reproduce Steps in the Paper	Lynn, Aly Khan	
Use Code to Reproduce Results from 3D Slicer/Image J	Manan, Yuheng, Jackson	Tues. Studio Block (Nov 19)

3-A. Client Meeting #6

Date: November 21, 2024

Attendance:
- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Lumeng Cui, Asieh Tavakol
- *Faculty Supervisor:* Tim Salcudean

Meeting Minutes

Topic #1: Feedback on Presentation

1) Do you guys have a better understanding of the workflow of the project?
    - Yes, going through the papers was very helpful, which allowed us to perform transformations and bias-field correction
    - It is important to see input and output images
2) Why would you need a Gaussian blurring?
    - Usually this just smooths out the image
    - Good thing is we can sometimes use to denoise
    - Downside is we lose a lot of details
    - Do not need to worry about the denoising part in our workflow, there are many methods already existing
    - Depends on what kernel set is being used
    - Relevant for implementation locally, not globally
    - Probably do not need to include in the workflow
3) What is the purpose of normalization?
    - Normalization (0 to 1), done correctly
    - Want to do this first, before inverse-logarithm scaling (Figure #X)
        - Want to keep intensity between 0 and 1 to keep the first part of the -log(image)
        - Want soft tissue to be dark for inverse log transform
        - If we do not control input by normalizing, the inverse log could be changed in the output
    - After loading image, need to do inverse logarithm
    - Image needs to be DICOM format

- Want to create threshold, using histogram after performing a gaussian fitting so we could obtain a ‘bone-only’ image
    - Can quickly pinpoint threshold after gaussian fitting

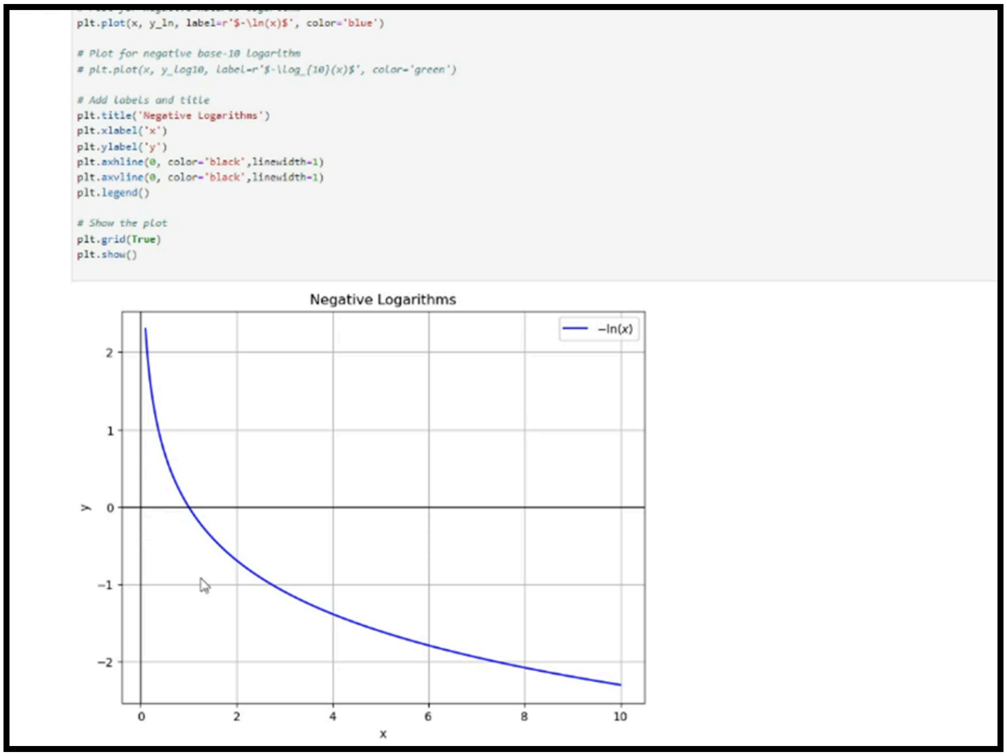

Figure A7. *Graph of Inverse Logarithmic Function.*

- Explore idea of how to implement a bias correction method that creates two narrow peaks within the histogram
- Gaussian fitting, is being applied to histogram to get a nice curve in order to determine the threshold which should be used
- After this we want to do histogram normalization
    - If your workflow works for chicken data and if given MR with human head data will be different, histogram normalization can help us to choose threshold in a standard way
    - For example, threshold will always be between 0.2 and 0.8 for bone

Topic #2: Critical Function Prototype

Image Segmentation

- Setting up threshold can be considered as segmentation process, able to differentiate between soft-tissue and background
- If threshold is chosen correctly should be able to segment out bone-only structure
- Not sure if it is reasonable to come up with deep-learning algorithm for such a short amount of time to the CFP presentation
- Once this is done, we can look into deep learning algorithm to use

Purpose of Deep Learning

- Improve segmentation technique
- Show chicken results, after histogram maybe manually do some thresholding
- First prototype, results will never look perfect but will show some progress
- Suggestion for deep learning, this stage may be too early to demonstrate
- Maybe just show deep learning literature review instead of specific applications

Table A11. *Action Items from the Sixth Client Meeting*

Actionable	***Persons Responsible***	***Deadline***
Perform Transformations in 3D Slicer	Lynn	Monday (Dec 25)
Document the Process for Testing & Verification	Aly Khan	Monday (Dec 25)
Implement the Code for Image Background Segmentation	Jackson, Manan	Monday (Dec 25)
Describe Key Functions of Prototype and Concept Selection	Yuheng	Monday (Dec 25)

3-B. Client Meeting #7

Date: November 26, 2024

Attendance:

- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Lumeng Cui, Gerry Moran

Questions:

- What is the best way to validate our results?
- Do we have the correct concepts for scoring?
- Does our function structure diagram correctly capture the workflow?

Meeting Minutes

Topic #1: Comments about CFP Presentation

- In general looks good, minor modifications needed
- For the normalization step [0,1]:
    - After performing bias correction we want to normalize data and then do inverse-logarithmic scaling
    - Do not need to rescale back to 255 intensity
        - For example, only resize if we want to export the image to DICOM format
    - Want every input image to be normalized from 0 to 1 regardless of the input
- Breakdown first section into more detailed steps
    - Save intermediate images by rescaling them to 255
    - Can export to 12-bit or 16-bit if more bit is needed
- Assumptions
    - First sentence: Mentions consistent spatial resolution
        - Idea is to work with images of any resolution
        - Want to make sure that when obtaining the image, the scan follows a standardized protocol (specifically UTE sequence)
        - Do not necessarily need consistent spatial resolution, as this would not be possible realistically
        - Without using UTE, bone signal is very small
        - If UTE is used, there will be a bone signal so we want to make sure that this is the case
    - Assumption is that the image must be acquired via UTE
    - Not sure about the second assumption:

        - Want to make sure workflow is robust enough that it is compatible with images from any MRI scanner
        - Instead say, "want to make sure workflow is robust enough that it can work with any scanner, but the scan protocol must be standardized"
            - Want TE and TR to be somewhat consistent
            - Although you are only provided with one dataset, the workflow is meant to be robust
- Limitations:
    - Elaborate on limitations to include future work so that any constraint is worked on or improved upon
    - Reword first sentence as follows: "right now we are only working with a limited number of data but once we have a concrete workflow, we will test the prototype with more datasets"
- With the current workflow (synthetic CT workflow), we want to use deep learning to improve the segmentation technique
- Testing:
    - Compare the bias-corrected and uncorrected image histograms to see if there are any noticeable improvements
    - N4ITK bias-field correction is likely not good enough
    - Might need to look at a different method/module, like the one mentioned in the first paper which used histogram intensity correction
    - After inverse log scaling, we want to make sure there are two narrow peaks
- Better if we show the images where the mask has been applied, not the mask itself
    - Apply the mask to the inverse log rescaled images
    - Also show the CT images for comparison
        - Try best to present CT images with matching orientations

Topic #2: Questions

<u>Do we have the correct FSD?</u>

- In the correct order
- Purpose of deep-learning
    - For the bone-tissue segmentation, we obtain synthetic CT output images
    - Only to make things better, not a mandatory component
- What is meant by artifact removal?
    - Some artifacts can easily be removed, sometimes easier to remove during acquisition
    - Remove this from the FSD as it is very dependent on the acquisition process of the images
- OpenRecon Display
    - Brand name for Siemens, if talking about this to our audience they may not know

- Swap this name for an 'On-scanner Display' instead
  - Not really open-source
  - Need framework or interface to be downloaded for support with MATLAB, or Python
  - On-scanner post-processing is often not possible
  - We want this workflow to be standardized and to be a real-time display for the images
- Segmentation
  - Compare synthetic output with real CT
  - Need registration to ensure that both images are in the same plane
  - Might not have enough time to implement this yet

<u>What is the best way to validate our results?</u>

- Look at DICE similarity score and structure similarity score (SSIM)
- Extract mask images and compare it between the sCT and the CT
- Same process for extracting the bone mask from the CT as from pCT
- Need registration for this step:
  - Either use automatic registration algorithm at the very beginning while registering MR and CT, or take output and register sCT to CT
  - Use 3D slicer or automatic registration in Python
- Visual inspection is also good
  - Comparing the bone in true CT and pCT
- In the future, introduce more metrics or criteria to have more quantitative comparison
- Want to make sure that there is a fair comparison:
  - Workflow or code needs to be modified to ensure this happens
- Compare histograms as a way to validate which should be visually very similar

<u>Do we have the correct concepts for scoring?</u>

- The concepts are probably good enough
- With GAN or U-Net they are commonly used and there is good amount of literature
- For example with U-Net this is used for segmentation all the time
- You do not know until you know so need to experiment for deep learning:
  - Only way is to train data with different models and see which performs best
- Criteria makes sense for now, however, might need to be revisited
- U-Net, 3D and 2D model
  - For this project, client probably cannot provide an extremely large dataset
  - 2.5D model: 1 3D dataset with each slice modelled in 2D
    - Training data with sagittal, coronal and axial plane makes it 2.5D
  - 2.5D works well and is probably good enough for machine learning

Table A12. *Action Items from the Seventh Client Meeting*

Actionable	***Persons Responsible***	***Deadline***
Complete the CFP Presentation	All	Wednesday (Nov. 27)
Perform Concept Scoring		Monday (Dec 2)

3-C. Client Meeting #8

Date: December 03, 2024

Attendance:

- *Capstone Team:* Aly Khan Nuruddin, Lynn Alvarez Krautzig, Yuheng Zhang, Manan Verma, Jackson Chen
- *Siemens Team:* Lumeng Cui, Asieh Tavakol

Questions:

- What are your thoughts on our budget? Do you anticipate any purchases to be made?

Meeting Minutes

Topic #1: Comments about Concept Screening, Scoring and Budget

- Client anticipates no urgent purchases to be made
- Can bring up any requests in the future with Gerry
- Must consider GPU resources for next term
    - Depends significantly on DL model that we decide to pursue
    - Cannot make a conclusive decision on computing resources at present moment
    - Do have individual computers to rely on for now

Topic #2: Presentation from Asieh

- Current workflow for radiotherapy:
    - CT has flat tabletop with external laser since positioning of the patient needs to be kept constant in the scanner during treatment
    - MRI and CT are fused for tumor and normal tissue delineation
    - Perform treatment planning and dose calculation on the CT image
- CT shows tumor and edema clearly but MRI does not
- MRI only workflow is needed since it has better soft tissue contrast without any exposure to ionizing radiation
- MRI cannot be used for dose calculation since intensities are based on proton density and magnetic relaxation of tissues
    - Electron densities are required to compute the ionizing doe
- Electron density phantom is a solid water disk for tissue characterization
- Need sCT from MRI data to inform radiation therapy planning for dose calculation

Table A13. *Action Items from the Eighth Client Meeting*

Actionable	***Persons Responsible***	***Deadline***

Finalize Midterm Budget Review	All	Thurs. Studio Block (Dec 5)
Complete DHFs 1-4		

6-A. Notes From Meeting with TA Fraser

Fault Tree Analysis (FTA) Considerations

- FTA may be more useful for identifying:
    - Most likely causes of failure
    - Most critical failure points
- Goal: Adapt the processing pipeline to be more robust
- Consider user error e.g., if non-MRI images are input:
    - What happens in this case?
    - Is this scenario already accounted for?
    - Is there a negative impact on output or performance?
- Use FTA as a thought framework:
    - Helps identify all potential failure points
    - If probabilities of failure are very low, pipeline changes may not be necessary
- Structure the fault tree as: *Program stops working → Why?*
    - Include subgroups linked to failure outcomes
    - Use logic gates (IF, AND, OR) to clarify dependencies
- Draft the fault tree before assigning probabilities
    - Focus efforts on the most critical branches
- Probability questions:
    - Are probabilities assigned at each module or higher-level branch?

    - Each block in the process should have an associated probability
    - Starting analysis from the top is generally recommended
- Action items:
    - Confirm with Tim about key ideas and probability assignment
    - Ask Tim whether justification is needed for choosing FTA over FMEA

Life-Cycle Assessment (LCA) Considerations

- Compare environmental costs of MRI vs. CT
- Assess the environmental impact of the algorithm itself:
    - Consider computational power and efficiency
    - Explore ways to improve energy efficiency
- If literature is lacking, estimate based on similar algorithms
- Potential justification: If a non-AI solution is equally effective, AI might not be environmentally justified
- Compare previous solutions to the proposed approach:
    - Suggest innovative alternatives, even if not the most sustainable
    - Consider overall net benefit vs. net negative
- Other specifications to consider:
    - Ability to run the program locally could be a valuable addition
    - FTA results might identify risky portions of the pipeline to address in LCA

9-A. NASA Task Load Index

Figure 8.6

NASA Task Load Index

Hart and Staveland's NASA Task Load Index (TLX) method assesses work load on five 7-point scales. Increments of high, medium and low estimates for each point result in 21 gradations on the scales.

Name	Task	Date

Mental Demand — How mentally demanding was the task?

Very Low — Very High

Physical Demand — How physically demanding was the task?

Very Low — Very High

Temporal Demand — How hurried or rushed was the pace of the task?

Very Low — Very High

Performance — How successful were you in accomplishing what you were asked to do?

Perfect — Failure

Effort — How hard did you have to work to accomplish your level of performance?

Very Low — Very High

Frustration — How insecure, discouraged, irritated, stressed, and annoyed wereyou?

Very Low — Very High

Figure A8. *NASA Task Load Index Survey*