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M.Sc Artificial Intelligence

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[RESEARCH PROPOSAL OUTLINE]

A brief outline of the research proposal on the topic of my capstone project

Project Title:

Deep Learning-Based Synthetic-Computed Tomography (sCT) Generation in Radiotherapy

Significance to the Research Problem:

Radiotherapy is a crucial treatment modality for cancer patients, relying heavily on accurate CT images for planning and dosage calculations. However, repeated CT scans can be harmful due to radiation exposure and are often not feasible in certain situations. The research problem lies in the need for a reliable method to generate synthetic CT images from other imaging modalities, such as Magnetic Resonance Imaging (MRI) or Cone Beam Computed Tomography (CBCT), to enhance the accuracy and safety of radiotherapy planning.

This research aims to address this problem by developing a deep learning-based approach to generate synthetic CT images, enabling more precise radiotherapy planning without the need for additional CT scans.

Research Question:

Can deep learning techniques be effectively employed to generate synthetic CT images from alternative imaging modalities in radiotherapy, and can these synthetic images achieve sufficient accuracy for treatment planning?

Aims and Objectives:

Aim 1: To develop a deep learning model for synthetic CT image generation.

Objective 1.1: Collect and preprocess a diverse dataset of MRI/CBCT and corresponding CT images.

Objective 1.2: Implement and train a deep neural network architecture for synthetic CT generation.

Objective 1.3: Evaluate the model's performance using quantitative and qualitative measures.

Aim 2: To assess the clinical utility and accuracy of synthetic CT images in radiotherapy planning.

Objective 2.1: Compare the synthetic CT images with actual CT images in terms of anatomical accuracy.

Objective 2.2: Analyse the impact of synthetic CTs on radiotherapy planning and dose calculations.

Objective 2.3: Assess the clinical feasibility and safety of using synthetic CTs in patient treatment.

Key Literature Related to the Project:

1. Spadea, M. F., Maspero, M., Zaffino, P., & Seco, J. (2021). Deep learning based synthetic-CT generation in radiotherapy and PET: A review. *Medical physics*, 48(11), 6537–6566. <https://doi.org/10.1002/mp.15150>
2. Liu, F., Yadav, P., Baschnagel, A. M., & McMillan, A. B. (2019). MR-based treatment planning in radiation therapy using a deep learning approach. *Journal of applied clinical medical physics*, 20(3), 105–114. <https://doi.org/10.1002/acm2.12554>
3. Bird, D., Nix, M. G., McCallum, H., Teo, M., Gilbert, A., Casanova, N., Cooper, R., Buckley, D. L., Sebag-Montefiore, D., Speight, R., Al-Qaisieh, B., & Henry, A. M. (2021). Multicentre, deep learning, synthetic-CT generation for ano-rectal MR-only radiotherapy treatment planning. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*, 156, 23–28. <https://doi.org/10.1016/j.radonc.2020.11.027>
4. Liu, Y., Lei, Y., Wang, T., Kayode, O., Tian, S., Liu, T., Patel, P., Curran, W. J., Ren, L., & Yang, X. (2019). MRI-based treatment planning for liver stereotactic body radiotherapy: validation of a deep learning-based synthetic

- CT generation method. *The British journal of radiology*, 92(1100), 20190067.
<https://doi.org/10.1259/bjr.20190067>
5. Maspero, M., Bentvelzen, L. G., Savenije, M. H. F., Guerreiro, F., Seravalli, E., Janssens, G. O., van den Berg, C. A. T., & Philippens, M. E. P. (2020). Deep learning-based synthetic CT generation for paediatric brain MR-only photon and proton radiotherapy. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*, 153, 197–204.
<https://doi.org/10.1016/j.radonc.2020.09.029>
 6. Shafai-Erfani, G., Wang, T., Lei, Y., Tian, S., Patel, P., Jani, A. B., Curran, W. J., Liu, T., & Yang, X. (2019). Dose evaluation of MRI-based synthetic CT generated using a machine learning method for prostate cancer radiotherapy. *Medical dosimetry : official journal of the American Association of Medical Dosimetrists*, 44(4), e64–e70.
<https://doi.org/10.1016/j.meddos.2019.01.002>
 7. Liu, Y., Lei, Y., Wang, Y., Shafai-Erfani, G., Wang, T., Tian, S., Patel, P., Jani, A. B., McDonald, M., Curran, W. J., Liu, T., Zhou, J., & Yang, X. (2019). Evaluation of a deep learning-based pelvic synthetic CT generation technique for MRI-based prostate proton treatment planning. *Physics in medicine and biology*, 64(20), 205022. <https://doi.org/10.1088/1361-6560/ab41af>
 8. Boulanger, M., Nunes, J. C., Chourak, H., Largent, A., Tahri, S., Acosta, O., De Crevoisier, R., Lafond, C., & Barateau, A. (2021). Deep learning methods to generate synthetic CT from MRI in radiotherapy: A literature review. *Physica medica : PM : an international journal devoted to the applications of physics to medicine and biology : official journal of the Italian Association of Biomedical Physics (AIFB)*, 89, 265–281.
<https://doi.org/10.1016/j.ejmp.2021.07.027>
 9. Barateau, A., De Crevoisier, R., Largent, A., Mylona, E., Perichon, N., Castelli, J., Chajon, E., Acosta, O., Simon, A., Nunes, J. C., & Lafond, C. (2020). Comparison of CBCT-based dose calculation methods in head and neck cancer radiotherapy: from Hounsfield unit to density calibration curve to deep learning. *Medical physics*, 47(10), 4683–4693.
<https://doi.org/10.1002/mp.14387>
 10. Cusumano, D., Lenkowicz, J., Votta, C., Boldrini, L., Placidi, L., Catucci, F., Dinapoli, N., Antonelli, M. V., Romano, A., De Luca, V., Chiloiro, G., Indovina, L., & Valentini, V. (2020). A deep learning approach to generate synthetic CT in low field MR-guided adaptive radiotherapy for abdominal and pelvic cases. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*, 153, 205–212.
<https://doi.org/10.1016/j.radonc.2020.10.018>
 11. O'Hara, C. J., Bird, D., Al-Qaisieh, B., & Speight, R. (2022). Assessment of CBCT-based synthetic CT generation accuracy for adaptive radiotherapy planning. *Journal of applied clinical medical physics*, 23(11), e13737.
<https://doi.org/10.1002/acm2.13737>
 12. Wang, T., Lei, Y., Manohar, N., Tian, S., Jani, A. B., Shu, H. K., Higgins, K., Dhabaan, A., Patel, P., Tang, X., Liu, T., Curran, W. J., & Yang, X. (2019). Dosimetric study on learning-based cone-beam CT correction in adaptive radiation therapy. *Medical dosimetry : official journal of the American Association of Medical Dosimetrists*, 44(4), e71–e79.
<https://doi.org/10.1016/j.meddos.2019.03.001>

13. Qiu, R. L. J., Lei, Y., Shelton, J., Higgins, K., Bradley, J. D., Curran, W. J., Liu, T., Kesarwala, A. H., & Yang, X. (2021). Deep learning-based thoracic CBCT correction with histogram matching. *Biomedical physics & engineering express*, 7(6), 10.1088/2057-1976/ac3055. <https://doi.org/10.1088/2057-1976/ac3055>
14. Chen, S., Peng, Y., Qin, A., Liu, Y., Zhao, C., Deng, X., Deraniyagala, R., Stevens, C., & Ding, X. (2022). MR-based synthetic CT image for intensity-modulated proton treatment planning of nasopharyngeal carcinoma patients. *Acta oncologica (Stockholm, Sweden)*, 61(11), 1417–1424. <https://doi.org/10.1080/0284186X.2022.2140017>
15. Chen, L., Liang, X., Shen, C., Jiang, S., & Wang, J. (2020). Synthetic CT generation from CBCT images via deep learning. *Medical physics*, 47(3), 1115–1125. <https://doi.org/10.1002/mp.13978>
16. Rusanov, B., Hassan, G. M., Reynolds, M., Sabet, M., Kendrick, J., Rowshanfarzad, P., & Ebert, M. (2022). Deep learning methods for enhancing cone-beam CT image quality toward adaptive radiation therapy: A systematic review. *Medical physics*, 49(9), 6019–6054. <https://doi.org/10.1002/mp.15840>
17. Chen, L., Liang, X., Shen, C., Nguyen, D., Jiang, S., & Wang, J. (2021). Synthetic CT generation from CBCT images via unsupervised deep learning. *Physics in medicine and biology*, 66(11), 10.1088/1361-6560/ac01b6. <https://doi.org/10.1088/1361-6560/ac01b6>
18. Lei, Y., Harms, J., Wang, T., Liu, Y., Shu, H. K., Jani, A. B., Curran, W. J., Mao, H., Liu, T., & Yang, X. (2019). MRI-only based synthetic CT generation using dense cycle consistent generative adversarial networks. *Medical physics*, 46(8), 3565–3581. <https://doi.org/10.1002/mp.13617>
19. Chen, X., Yang, B., Li, J., Zhu, J., Ma, X., Chen, D., Hu, Z., Men, K., & Dai, J. (2021). A deep-learning method for generating synthetic kV-CT and improving tumor segmentation for helical tomotherapy of nasopharyngeal carcinoma. *Physics in medicine and biology*, 66(22), 10.1088/1361-6560/ac3345. <https://doi.org/10.1088/1361-6560/ac3345>
20. Farjam, R., Nagar, H., Kathy Zhou, X., Ouellette, D., Chiara Formenti, S., & DeWyngaert, J. K. (2021). Deep learning-based synthetic CT generation for MR-only radiotherapy of prostate cancer patients with 0.35T MRI linear accelerator. *Journal of applied clinical medical physics*, 22(8), 93–104. <https://doi.org/10.1002/acm2.13327>
21. Deng, L., Ji, Y., Huang, S., Yang, X., & Wang, J. (2023). Synthetic CT generation from CBCT using double-chain-CycleGAN. *Computers in biology and medicine*, 161, 106889. <https://doi.org/10.1016/j.combiomed.2023.106889>
22. Liu, X., Emami, H., Nejad-Davarani, S. P., Morris, E., Schultz, L., Dong, M., & K Glide-Hurst, C. (2021). Performance of deep learning synthetic CTs for MR-only brain radiation therapy. *Journal of applied clinical medical physics*, 22(1), 308–317. <https://doi.org/10.1002/acm2.13139>
23. Lemus, O. M. D., Wang, Y. F., Li, F., Jambawalikar, S., Horowitz, D. P., Xu, Y., & Wu, C. S. (2022). Dosimetric assessment of patient dose calculation on a deep learning-based synthesized computed tomography image for adaptive radiotherapy. *Journal of applied clinical medical physics*, 23(7), e13595. <https://doi.org/10.1002/acm2.13595>
24. Liu, Y., Chen, X., Zhu, J., Yang, B., Wei, R., Xiong, R., Quan, H., Liu, Y., Dai, J., & Men, K. (2022). A two-step method to improve image quality of CBCT

- with phantom-based supervised and patient-based unsupervised learning strategies. *Physics in medicine and biology*, 67(8), 10.1088/1361-6560/ac6289. <https://doi.org/10.1088/1361-6560/ac6289>
25. Wu, W., Qu, J., Cai, J., & Yang, R. (2022). Multiresolution residual deep neural network for improving pelvic CBCT image quality. *Medical physics*, 49(3), 1522–1534. <https://doi.org/10.1002/mp.15460>
 26. Lerner, M., Medin, J., Jamtheim Gustafsson, C., Alkner, S., Siversson, C., & Olsson, L. E. (2021). Clinical validation of a commercially available deep learning software for synthetic CT generation for brain. *Radiation oncology (London, England)*, 16(1), 66. <https://doi.org/10.1186/s13014-021-01794-6>
 27. Lenkowicz, J., Votta, C., Nardini, M., Quaranta, F., Catucci, F., Boldrini, L., Vagni, M., Menna, S., Placidi, L., Romano, A., Chiloire, G., Gambacorta, M. A., Mattiucci, G. C., Indovina, L., Valentini, V., & Cusumano, D. (2022). A deep learning approach to generate synthetic CT in low field MR-guided radiotherapy for lung cases. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*, 176, 31–38. <https://doi.org/10.1016/j.radonc.2022.08.028>
 28. Aouadi, S., Yoganathan, S. A., Torfeh, T., Paloor, S., Caparrotti, P., Hammoud, R., & Al-Hammadi, N. (2023). Generation of synthetic CT from CBCT using deep learning approaches for head and neck cancer patients. *Biomedical physics & engineering express*, 9(5), 10.1088/2057-1976/acea27. <https://doi.org/10.1088/2057-1976/acea27>
 29. Zhang, Y., Yue, N., Su, M. Y., Liu, B., Ding, Y., Zhou, Y., Wang, H., Kuang, Y., & Nie, K. (2021). Improving CBCT quality to CT level using deep learning with generative adversarial network. *Medical physics*, 48(6), 2816–2826. <https://doi.org/10.1002/mp.14624>
 30. Kaushik, S. S., Bylund, M., Cozzini, C., Shanbhag, D., Petit, S. F., Wyatt, J. J., Menzel, M. I., Pirkl, C., Mehta, B., Chauhan, V., Chandrasekharan, K., Jonsson, J., Nyholm, T., Wiesinger, F., & Menze, B. (2023). Region of interest focused MRI to synthetic CT translation using regression and segmentation multi-task network. *Physics in medicine and biology*, 68(19), 10.1088/1361-6560/acefa3. <https://doi.org/10.1088/1361-6560/acefa3>
 31. Gjestebj, L., Shan, H., Yang, Q., Xi, Y., Jin, Y., Giantsoudi, D., Paganetti, H., De Man, B., & Wang, G. (2019). A dual-stream deep convolutional network for reducing metal streak artifacts in CT images. *Physics in medicine and biology*, 64(23), 235003. <https://doi.org/10.1088/1361-6560/ab4e3e>
 32. Thummerer, A., Sella Ori, C., Zaffino, P., Meijers, A., Guterres Marmitt, G., Wijsman, R., Seco, J., Langendijk, J. A., Knopf, A. C., Spadea, M. F., & Both, S. (2021). Clinical suitability of deep learning based synthetic CTs for adaptive proton therapy of lung cancer. *Medical physics*, 48(12), 7673–7684. <https://doi.org/10.1002/mp.15333>
 33. Shields, B., & Ramachandran, P. (2023). Generating missing patient anatomy from partially acquired cone-beam computed tomography images using deep learning: a proof of concept. *Physical and engineering sciences in medicine*, 46(3), 1321–1330. <https://doi.org/10.1007/s13246-023-01302-y>
 34. Tien, H. J., Yang, H. C., Shueng, P. W., & Chen, J. C. (2021). Cone-beam CT image quality improvement using Cycle-Deblur consistent adversarial networks (Cycle-Deblur GAN) for chest CT imaging in breast cancer patients. *Scientific reports*, 11(1), 1133. <https://doi.org/10.1038/s41598-020-80803-2>

35. Xue, X., Ding, Y., Shi, J., Hao, X., Li, X., Li, D., Wu, Y., An, H., Jiang, M., Wei, W., & Wang, X. (2021). Cone Beam CT (CBCT) Based Synthetic CT Generation Using Deep Learning Methods for Dose Calculation of Nasopharyngeal Carcinoma Radiotherapy. *Technology in cancer research & treatment*, 20, 15330338211062415. <https://doi.org/10.1177/15330338211062415>
36. Arabi, H., Dowling, J. A., Burgos, N., Han, X., Greer, P. B., Koutsouvelis, N., & Zaidi, H. (2018). Comparative study of algorithms for synthetic CT generation from MRI: Consequences for MRI-guided radiation planning in the pelvic region. *Medical physics*, 45(11), 5218–5233. <https://doi.org/10.1002/mp.13187>
37. Yuan, N., Rao, S., Chen, Q., Sensoy, L., Qi, J., & Rong, Y. (2022). Head and neck synthetic CT generated from ultra-low-dose cone-beam CT following Image Gently Protocol using deep neural network. *Medical physics*, 49(5), 3263–3277. <https://doi.org/10.1002/mp.15585>
38. Wyatt, J. J., Kaushik, S., Cozzini, C., Pearson, R. A., Petit, S., Capala, M., Hernandez-Tamames, J. A., Hideghéty, K., Maxwell, R. J., Wiesinger, F., & McCallum, H. M. (2023). Comprehensive dose evaluation of a Deep Learning based synthetic Computed Tomography algorithm for pelvic Magnetic Resonance-only radiotherapy. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*, 184, 109692. <https://doi.org/10.1016/j.radonc.2023.109692>
39. Handrack, J., Bangert, M., Möhler, C., Bostel, T., & Greilich, S. (2020). Towards a generalised development of synthetic CT images and assessment of their dosimetric accuracy. *Acta oncologica (Stockholm, Sweden)*, 59(2), 180–187. <https://doi.org/10.1080/0284186X.2019.1684558>
40. Gao, L., Xie, K., Wu, X., Lu, Z., Li, C., Sun, J., Lin, T., Sui, J., & Ni, X. (2021). Generating synthetic CT from low-dose cone-beam CT by using generative adversarial networks for adaptive radiotherapy. *Radiation oncology (London, England)*, 16(1), 202. <https://doi.org/10.1186/s13014-021-01928-w>
41. Olberg, S., Zhang, H., Kennedy, W. R., Chun, J., Rodriguez, V., Zoberi, I., Thomas, M. A., Kim, J. S., Mutic, S., Green, O. L., & Park, J. C. (2019). Synthetic CT reconstruction using a deep spatial pyramid convolutional framework for MR-only breast radiotherapy. *Medical physics*, 46(9), 4135–4147. <https://doi.org/10.1002/mp.13716>
42. Neppl, S., Landry, G., Kurz, C., Hansen, D. C., Hoyle, B., Stöcklein, S., Seidensticker, M., Weller, J., Belka, C., Parodi, K., & Kamp, F. (2019). Evaluation of proton and photon dose distributions recalculated on 2D and 3D Unet-generated pseudoCTs from T1-weighted MR head scans. *Acta oncologica (Stockholm, Sweden)*, 58(10), 1429–1434. <https://doi.org/10.1080/0284186X.2019.1630754>
43. Neppl, S., Landry, G., Kurz, C., Hansen, D. C., Hoyle, B., Stöcklein, S., Seidensticker, M., Weller, J., Belka, C., Parodi, K., & Kamp, F. (2019). Evaluation of proton and photon dose distributions recalculated on 2D and 3D Unet-generated pseudoCTs from T1-weighted MR head scans. *Acta oncologica (Stockholm, Sweden)*, 58(10), 1429–1434. <https://doi.org/10.1080/0284186X.2019.1630754>
44. Kurz, C., Maspero, M., Savenije, M. H. F., Landry, G., Kamp, F., Pinto, M., Li, M., Parodi, K., Belka, C., & van den Berg, C. A. T. (2019). CBCT correction using a cycle-consistent generative adversarial network and unpaired training

- to enable photon and proton dose calculation. *Physics in medicine and biology*, 64(22), 225004. <https://doi.org/10.1088/1361-6560/ab4d8c>
45. Szmul, A., Taylor, S., Lim, P., Cantwell, J., Moreira, I., Zhang, Y., D'Souza, D., Moinuddin, S., Gaze, M. N., Gains, J., & Veiga, C. (2023). Deep learning based synthetic CT from cone beam CT generation for abdominal paediatric radiotherapy. *Physics in medicine and biology*, 68(10), 105006. <https://doi.org/10.1088/1361-6560/acc921>
 46. Koide, Y., Shimizu, H., Wakabayashi, K., Kitagawa, T., Aoyama, T., Miyauchi, R., Tachibana, H., & Kodaira, T. (2021). Synthetic breath-hold CT generation from free-breathing CT: a novel deep learning approach to predict cardiac dose reduction in deep-inspiration breath-hold radiotherapy. *Journal of radiation research*, rrab075. Advance online publication. <https://doi.org/10.1093/jrr/rrab075>
 47. Fu, J., Yang, Y., Singhrao, K., Ruan, D., Chu, F. I., Low, D. A., & Lewis, J. H. (2019). Deep learning approaches using 2D and 3D convolutional neural networks for generating male pelvic synthetic computed tomography from magnetic resonance imaging. *Medical physics*, 46(9), 3788–3798. <https://doi.org/10.1002/mp.13672>
 48. Maspero, M., Houweling, A. C., Savenije, M. H. F., van Heijst, T. C. F., Verhoeff, J. J. C., Kotte, A. N. T. J., & van den Berg, C. A. T. (2020). A single neural network for cone-beam computed tomography-based radiotherapy of head-and-neck, lung and breast cancer. *Physics and imaging in radiation oncology*, 14, 24–31. <https://doi.org/10.1016/j.phro.2020.04.002>
 49. Yousefi Moteghaed, N., Mostaar, A., & Azadeh, P. (2021). Generating pseudo-computerized tomography (P-CT) scan images from magnetic resonance imaging (MRI) images using machine learning algorithms based on fuzzy theory for radiotherapy treatment planning. *Medical physics*, 48(11), 7016–7027. <https://doi.org/10.1002/mp.15174>

Research Design:

Data Collection: Gather a diverse dataset of paired MRI/CBCT and CT images from previous patients.

Data Preprocessing: Standardise and preprocess the data, including image registration and segmentation.

Deep Learning Model: Develop a deep neural network architecture, such as a convolutional neural network (CNN), for synthetic CT generation.

Training and Validation: Train the model on the dataset and validate its performance using metrics like mean squared error and structural similarity index.

Clinical Evaluation: Assess the utility of synthetic CT images in radiotherapy planning through a comparative study with actual CT images.

Ethical Approval: Seek ethical approval for the use of patient data and ensure compliance with data protection regulations.

Ethical Considerations and Risk Assessment:

Ethical approval will be sought to ensure patient data privacy and confidentiality.

Risks associated with the project include potential errors in synthetic CT generation that could impact treatment planning. These risks will be mitigated through rigorous validation and clinical assessment. Informed consent will be obtained for the use of patient data.

Description of Artefact:

The primary artefact of this research will be a deep learning model capable of generating synthetic CT images from MRI data. Additionally, the research will produce a comprehensive report detailing the model's development, evaluation, and its potential impact on radiotherapy planning.

Timeline of Proposed Activities:

Month 1: Data collection and preprocessing

Month 1-2: Model development and training

Month 3: Model validation and performance evaluation

Month 4: Clinical assessment and ethical approval application

Month 4-5: Final analysis and report writing

Month 5-6: Dissemination of research findings and potential publication

Conclusion:

This proposed research aims to make a significant contribution to the field of radiotherapy by providing a reliable and safe method for generating synthetic CT images, ultimately improving the accuracy and quality of patient treatment planning.