

# Deep Learning for Radiation Dose Estimation

Masterarbeit

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## Abstract

Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

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# Abkürzungsverzeichnis

# 1 Introduction

## Introduction

- **Genereller Ablauf am MR-Linac stand jetzt**
- Person kommt, bekommt ein CT für initiale Planung, danach wird dann bei Bestrahlung des Patienten ein MRT von dem Patienten gemacht. Registrierung von CT und MRT und adaption von contours auf MRT. Dann Online-Plan adaption bei dem Plan aufgrund von adapt to position oder shape. Results in no adaption or adaption of segments shape, monitor units or both. This is repeated for each treatment fraction of the patient (Adaptive radiotherapy: The Elekta Unity MR-linac concept)
- **Wie soll der Ablauf einmal aussehen beim MR-Linac**
- Goal is to achieve a MRi-only treatment workflow, including imaging with MRI contouring on MRI and planning and calculation of plans on mri. dose calculation is not possible on mri data because mri is not a quantitative imaging modality, meaning pixel values give no information about the electron density of the underlying tissue or body part. therefore synthetic ct images need to be created from mri images, which enable dose calculations.
- **Und dann auf Dosisdeposition eingehen / Was ist aktuelle Methode** hier noch viel verschieben nach material und methodik
- (<http://dx.doi.org/10.1118/1.2795842>) monte carlo simulations are currently used for dose calculation for radiotreatment plans in a clinical setting. The interactions of photons in human tissue in the energy spectrum of interest for external beam therapy transfer the photon energy on to electrons or positrons. these particles then transfer their energy into the surrounding tissue. before energy deposition the photon and especially the electron undergo a number of elastic and non elastic interactions with atoms. In the process the main energy loss is caused by inelastic collisions and radiative interactions. the collisions result in ionization and therefore secondary electrons. radative interactions result in a energy trasnfer back to photons. the sum of these phenomena in a photon field results in a coupled electron-photon shower, which can be described by a coupled set of integrodifferential transport equations. due to the lack of a analytical solution, without any major simplifications and assumptions for conditions, the monte carlo algorithm is

used to simulate a multitude of particle histories in the desired target volume. partical histories describe the exact way of a photon from the source to its point in the volume were it has lost all of its energy including enery transport to secondary electrons in the process of collisions. the stochastic nature of the interaction processes of photons and electrons need for a large number of simulated particles to achieve an accurate result of dose deposition. the entirety of all simulated particles then results in an accurate dose distribution which can be used for treatment planning. the need for particle histories in the magnitude of  $10^7$  to  $10^{11}$  for accurate dose estimations, result in long simulation times.

- Wo findest Deep Learning Anwendung (Bezug zu Medizin)
- Deep learning and especially computer vision is already present in current research of Biology, Physics as well as medicine. there are a multiple fields in which CV can be applied to fields such as dermatology (<https://sci-hub.ru/10.1038/nature21056>), radiology (<https://sci-hub.ru/10.1038/srep24454>, <https://sci-hub.ru/10.1097/rli.0000000000000000>), cardiology (<https://arxiv.org/abs/1708.09843>) or pathology (<https://www.nature.com/articles/020-58467-9.pdf>)
- Einleitung zu Deep Learning
- . deep learning is a prefered tool due to its short inference times aswell as super human performance level on certain tasks. the implementation of the fully convulitional network (<https://arxiv.org/pdf/1411.4038.pdf>) and its further development of the U-Net utilizing data from higher level representations of the data in the form of skip connections (<https://arxiv.org/abs/1505.04597>) have revolutionized the application of deep learning for image data and 3d data i the form of a 3D-UNets.
- Was ist die Contribution / Aims <- Ziel: Dosisvorhersage mit DL, möglichst robust
- In this paper we investiage the capabilities of deep learning in the field of dose predictions for radio treatment plans. we aimed to achieve a robust dose prediction irrespective of the body region of interest and irresprective of the complexity of the treatment plan.
- 

Show why Radiotherapy is so important: search for sources of application of radiotherapy for different entities. Prostate: [1–3] Mamma: [4–6] Head & Neck: [7–10] Liver: [11–15] Lymph Nodes: [16–20]



Was ich noch brauche: Infos über MR-Linac, was ist die Vision hinter dem MR Linac (online adaption)

The use of Magnet Resonance Imaging (MRI) during radiotherapy has opened a variety of new opportunities for treatment optimization. MRI provides a better contrast in soft tissue areas of the body, compared to conventional computed tomography (CT), and can be used to assess functional image data from the patient in real time. The enhanced contrast leads to better organs at risk (OAR) and tumor volume delineation. (doi:10.1016/S0360-3016(03)01446-9). Recent research efforts are exploring the capabilities of the hybrid MRI linear accelerator (MRI-Linac) (doi:10.1007/s00066-018-1386-z, doi:10.1016/j.radonc.2007.10.034, doi:10.1002/acm2.12233). The introduction of the MRI-Linac has transformed the clinical workflow for radiotherapy as well as treatment planning. Patients are required to receive one CT for initial treatment planning. For radiation in each fraction, the initial plan is registered on the current MRI and optionally adapted to shift or size variation of the tumor volume (doi:10.1016/j.ctro.2019.04.001). Goal is to reach an MRI-only-workflow where image acquisition, treatment planning and radiotherapy only involve the MRI-Linac. To achieve this goal multiple steps in the clinical workflow need to be adapted

behind MRI Linac is an radiotreatment adaption in an online manner, meaning that a shift of the tumor volume and changes to the patients anatomy due to movement can be considered to adapt the treatmentplan. This results in smaller safety margins (doi:10.1102/1470-7330.2004.0054) for tumor volumes and ultimately result in a lower delivered dose to organs at risk. To achieve this ultimate goal, multiple steps, such as anatomy segmentation, treatmentplan adaption and dose deposition simulations need to be able to be performed in real-time.

Welche besonderheiten gibt es bei einem MR-Linac im Vergleich zu einem normalem Bestraher (Stichworte: ERE, Electron Deposition Shift) Wie funktioniert normale Dosisberechnung (Monte Carlo doi:10.1118/1.598917), warum ist der Nutzen davon limitiert wenn man in die online Adaption möchte.

However, since MC simulation is a stochastic process, the resulting dose map contains inherent quantum noise whose variance is inversely proportional to the number of the simulation histories and, accordingly, to the simulation time. Typically, achieving clinically acceptable precision requires hours of CPU computation time. Graphics processing unit (GPU)-based parallel computation frameworks can accelerate MC simulation to a few minutes for a typical IMRT/VMAT plan (doi:10.1088/0031-9155/55/11/006)

However, several areas in the clinical workflow require real-time dose calculation, such as

inverse optimization of the treatment planning process for IMRT and VMAT (doi:10.1088/2632-2153/abdbfe) especially online radiotherapy and online plan adaption are limited by the time needed to recalculate dose distributions of beam settings and patient anatomies due to moving organs (doi:10.1016/j.clon.2018.08.001)

Machine Learning Teil: Wie wird Machine Learning in verschiedenen bereichen der bestrahlungsplanung bezüglich MRI genutzt: Eine Implementierung und Nutzung dieser könnte zum Erreichen einer Online-Bestrahlungsadaption führen

1. Autosegmentation ([21, 22]) aswell as uncertainty ([23])
2. Radio Treatment Plan optimization ([24, 25])
3. Dose Estimation ([26, 27] active denoising of lower history MC Simulations (doi:10.1002/mp.13856))
4. Pseudo CT ([28–30])

## 2 Previous Work

Previous Work (evtl. mit in die Introduction) / Related Work

- Bezug nehmen auf
- DeepDose
- Weitere Paper zu dem Thema (Protonen mit LSTM, weitere Dosisberechnungen, siehe Paper, dass Christian gesendet hat)

Radiotherapy:

**<https://iopscience.iop.org/article/10.1088/1361-6560/ab7630>**

using 3d unet architecture and patch based approach to estimate dose in prostate cancer patients for individual segments of an entire treatmentplan. input data fro unet include patient information in the form of ct, as well as information form the accellerator such as beam angle and beam shape. they achieve very good results with  $99.9 \pm 0.3$  for 3%/3mm gamma passrate. and 1 minute for dose estimation for one patient in total

**<https://aapm.onlinelibrary.wiley.com/doi/full/10.1002/mp.14658>**

dose prediction for protonfields in highly heterogenous tissues using long short term memory (LSTM) networks. it treats the affected part of the tissue as a sequence of 2 inputs and calculates the respective dose in the scheme of a marching beam trough the tissue. the reach robustnes by generating artificial phantom cases for the dose predictions. results show 98.57% gamma passrate (1%/3mm) for artificial cases and an average gama passrate of 97.85% for patient test cases.

**<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7870566/>**

dose estimation for segments was achieved by combining fluence maps from segments aswell as patient anatomies. they generated 3d fluence volumes from 2d fluence maps including information of beam angle. an 3d unet like architecture with residual blocks inside the convolutional building block was used for prediction. the overall dose variation normalized to the prescribed dose was  $0.17\% \pm 2.28\%$ .

### **High-Particle Simulation of Monte-Carlo Dose Distribution with 3D ConvLSTMs**

to achieve a precise dose distribution in the desired 3d volume they use an approach utilizing active denoising of monte carlo simulations with deep learning. they implemented a 3d LSTM architecture inside the skipconnection of a 3d unet architecture. a sequence of noisy monte carlo simulations was used as the input and the output is the denoised

doe prediction. the loss function was constructed from the L1 loss and the structural similarity index measure. gamma pass rate for 5 patients was  $94.1\% \pm 1.2\%$  and the L1 was  $4 \cdot 10^{-3} \pm 1 \cdot 10^{-3}$ .

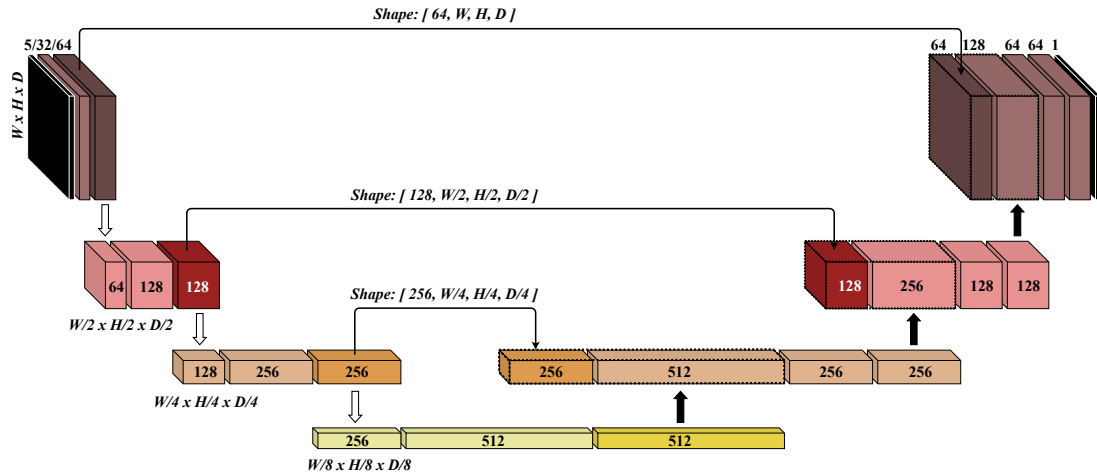
**DeepMCDose: A Deep Learning Method for Efficient Monte Carlo Beamlet Dose Calculation by Predictive Denoising in MR-Guided Radiotherapy** the proposed network consists of 3 seperate Unets to seperately analyse the 3 input channels consisting of unsampled MC dose, MC x-ray fluence and the ct geometry for a single beamlet. the output from each network is then combined to calculate the residual needed dose to achieve the denoised dose distribution. the normalized mean absolute error reduced from 25.7% on the undersamplet MC simulation to 0.106% for the network output. The simulation of 380s for an fully sampled beamlet was reduced to 220 ms for the network prediction

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7115345/>

### 3 Medical Knowledge

Medical Base Knowledge:

wieso schreibe ich hier über radiotherapy - wie wird sie angewendet - was ist konverntionell  
- linear beschleuniger, ablauf für patienten - planung dosis nebenwirkungen eingehen - auf  
was zielt der MR linac ab überleitung zu dosisberechnungs algorithmen - monte carlo - in  
detail EGSnrc eingehen und erläutern was der vorteil hier für uns ist (einzelne segmente,  
erläuterung, dass ein plan aus verschiedenen segmenten besteht die aufsummiert werden)  
kurz über wechselwirkungen reden und wie die dosisdeposition mit monte carlo simuliert  
wird. dann kurz erläutern warum ich das hier eigentlich grade beschreibe - darauf eingehen  
dass trainingsdaten halt mit diesem egsrc simuliert werden



**Figure 1:** Network architecture scheme. Size of the input masks are depicted by width (W), height (H) and depth (D). Input dimensionality is  $W \times H \times D \times 5$  and output dimensionality is  $W \times H \times D \times 1$ .

## 4 Material and Methods

Material and Methods (Unsicher wie ich das aufbauen soll)

Netzwerk Architektur Dataloading Was ist Input Wie werden Trainingsdaten erzeugt Auswertungsmetriken

- Hypothesen und wie wir diese Überprüfen: - ...

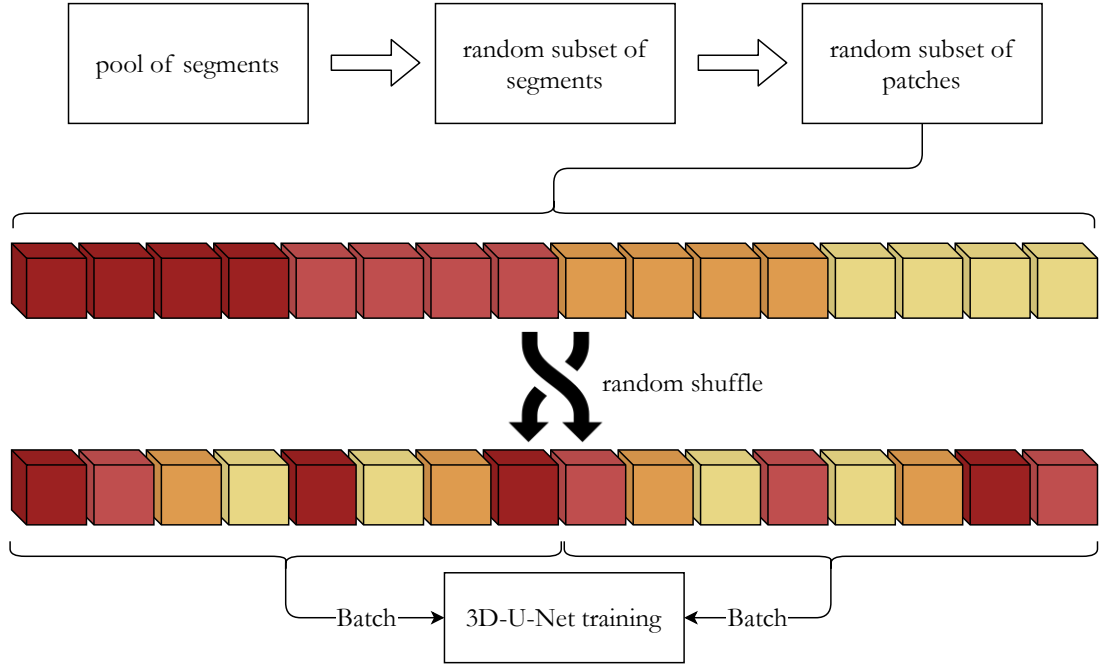
Data: Beschreibung der Patientendaten (wie viele, wie verteilt) Infos zu der Ethical... Falls in der Discussion die Feldgröße von Relevanz ist dann Infos mit rein nehmen. Nähere Infos in Tabelle

### 4.1 Network Architecture

3D UNet architecture with a downsampling ratio of 8 and a maximum layer depth of 512 in the bottleneck connection and skip connections before each pooling layer. multiple input masks in the size of CT with a resolution of  $1.1718 \times 1.1718 \times 3 \text{ mm}^3$  resolution in coronal, sagittal, and transversal dimension respectively. shown in image fig. 1

### 4.2 Dataloading

Patch based training, warum erklären, dass aufgrund der Natur von 3D-Daten und dem Limit des Grafikkarten speichers nur ein teil der daten geladen werden können. erklären, dass der speicherplatz verbrauch zum vorherigen abspeichern aller patches zu groß ist



**Figure 2:** Memory efficient queue based dataloading for 3D patch based training. data from different segments are depicted in different color shades.

und die patches somit on the fly extrahiert werden müssen. eingehen auf TorchIO und deren lösung mittels einer queue an der sich meine lösung orientiert. on the fly loading von den daten in den datenspeicher und dann nach und nach füttern des Netzwerks mit gemischten Patches von verschiedenen patienten. verweis auf fig. 2

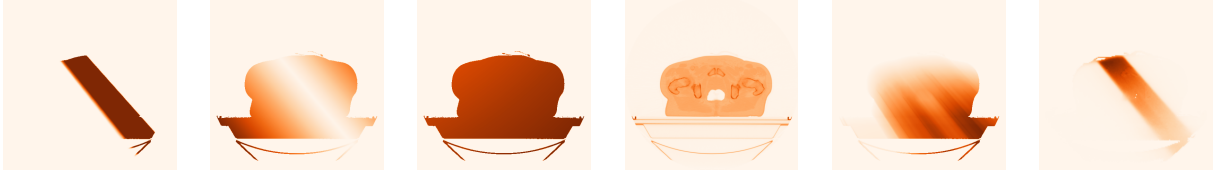
## 4.3 Network Input & Output

### 4.3.1 Network Input

The input consists of 5 3D volumes (fig. 3) to combine different spatial, anatomical as well as accelerator information into the training data. the masks are used to achieve a direct connection from accelerator that translates onto the patients anatomy

**Beam Shape:** beam shape information in form of a volume indicating the trajectory of the beam and its specific shape for each segment. in the masks voxels which the trajectory passes contain the beam area. this accounts for the output factor of the accelerator, meaning that for bigger fields the in-scatter in the central beam line is higher than for smaller fields.

**Center Beam Line Distance:** The beam of a linear accelerator is best defined in the



**Figure 3:** From left to right: Beam Shape Mask, Center Beam Line Distance Mask, Source Distance Mask, CT Mask, Radiological Depth, Target Dose Mask

central beam line. therefore the distance from the central beam line is of importance for the dose deposition. the minimum distance of each voxel from the central beam line accounting voxel dimensionality is saved in this mask.

**Source Distance:** The square rule of distance for the tissue in which the photons interact and the radiation source is of crucial importance for the dose deposited in the affected tissue. the values in this mask reflect the distance from each voxel to the radiation source with accounting the voxel dimensionality.

**CT:** Dose deposition and particle interaction in genereal are defined by their energy aswell as the electron density of the affected volume. as the energy of the radiated photons is constant, the impact of the electron density of the volume (in this case the patients anatomy) is accounted in this mask. It consits of the hounsfield units from a ct scan. with this mask dose deposition in denser tissues can be accounted for.

**Radiological Depth:** as a particle passes trough the affected volume it loses its energy on its path. therefore the depth, which a particle has already passedd inside a tissue is very important for the dose deposition effects that take place. because particles lose their energy faster in dense materials, this affect is accounted for using the radiological depth. it accounts for the distance from the source as well as the electron density of the passed tissue. A depth in a dense material results in a higher radiological depth that the same depth in soft tissue.

To only clip the mask values to the actual patients anatomy, all values in each mask were set to zero where the CT mask had a HU value smaller than 874 (150 values above the HU value for air).



### 4.3.2 Network Output

The output yielded by the network is the single volume of the predicted dose for the given input. It has the same dimensionality for width height and depth as well as voxel dimensions as the input masks. shown in fig. 3

## 4.4 Training Data Generation

The patient anatomy and accelerator information of each segment was extracted from the radio treatment plan. The required masks were created from this information using in-house python scripts. The target dose mask was simulated using the dosxyznrc software tool from the EGSnrc software package (the code is publicly available at <https://github.com/nrc-cnrc/EGSnrc>). EGSnrc enabled us to simulate each beam segment from each patient's treatment plan, with the accurate MR linac accelerator head model from previous work at our institution. Each segment was simulated using  $10^7$  for time efficiency.

hier noch beschreiben wie lange die daten generation braucht? wichtig?

## 4.5 Evaluation Metrics

to directly assess the quality of the dose prediction, we used the gamma - passrate, which compares two dose distributions on the same grid. in this analysis tool each voxel and its value on grid 1 is compared to the corresponding voxel from the second dose distribution. two margins are used that define in which margin the second dose voxel can vary to be accepted as valid. the two margins are a dose value margin as well as a spatial margin. hier noch erklären was der spatial margin eigentlich aussagt

hier noch vllt formel und abbildung die auswertungsmetrik

## 4.6 Hypotheses

**These 1:** the general dose deposition process for a specific tumor entity can be learned on data of a multitude of radio treatment plans on that the specific tumor site. We therefore train a network on prostate patient treatment plan data and anatomies and assess the quality of predicted dose distribution with the gamma passrate of each segment as well as the entire plan.

**These 2:** the in These 1 trained network performs poorly when translating into different tumor sites that were not included in the training data and therefore generalizes poorly.

To test translational capabilities the network is tested against liver, breast, head & neck and lymph node treatment plan data.

**These 3:** the inclusion of different tumor sites into the training data improves the the translational capabilities of the network to other tumor sites, while maintaining high accuracy on the included tumor sites and therefore improve the robustness of the network. we therefore train the same network from these 1 on prostate, liver, breast and head & neck treatment plan data. the translational capabilities are then assed by testing with prostate, liver, breast, head & neck and lymph node data. by doing this we asses if the network performance decreases on prostate data by including new tumor sites into the training data and we assess its performance on seen (prostate, liver, head & neck, breast) aswell as unseen treatment plan data (lymph nodes).

**These 4:** The network is capable of learning the underlying physics of the dose deposition process. By creating phantom input data in the form of a water slab at various positions inside an air volume, we investigate if the network has learned the underlying physics of the dose deposition process.

## 4.7 Patient Data

patient data from our institution previously treated at the mr linac. all plans were created by a medical physicist in agreement with a oncologist Welche Entitäten: Prostate only training: 45 prostate treatment plans with a total of 2342 Segments, 36/4/5 split für train / val / test split. with a mean fieldsize of  $36.57 \pm 17.9 \text{ cm}^2$  for training / validation set and  $34.57 \pm 15.86 \text{ cm}^2$  for the test set. mixed model 15 prostate with 720 segments ,  $35.49 \pm 18.01$  and  $34.57 \pm 15.86$  15 liver 819 Segments  $24.09 \pm 18.36$  and  $22.81 \pm 14.47$  15 mamma 656 Segments  $40.72 \pm 28.48$  and  $40.60 \pm 37.98$  14 head & neck 929 segments in einem 8/2/5 split also in 32/8/20 train / validation / test ratio. aswell as 15 patient plans 659 segments for lymphnodes exclusively for testing with a mean fieldsize of  $25.95 \pm 25.59$  as you can see in tab. 1

$63.00 \pm 50.47$   $68.89 \pm 53.56$

Prostate-Only		Mixed-Entity				Testing
		Liver	Mamma	Head & Neck	Prostate	Lymphnodes
Number of Segments	45	15	15	15	15	15
Number of Segments	2342	819	656	929	720	659
Training / Validation / Testing	36/4/5	8/5/2	8/2/5	8/5/2	8/5/2	Only Testing
Fieldsize Training/Validation	36.5 (17.9)	24.1 (18.4)	40.7 (28.5)	63.0 (50.5)	35.5 (18.0)	N/A
Fieldsize Testing	34.5 (15.8)	22.8 (14.4)	40.6 (38.0)	68.9 (53.6)	34.6 (15.9)	26.0 (25.6)

**Table 1:** Patient data information for Prostate-Only as well as Mixed-Entity trained model and testing data set. Fieldsizes are given as mean (standard deviation).

## Literature

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## Apendix