A dedicated software application for treatment verification with off-line PET/CT imaging at the Heidelberg Ion Beam Therapy Center

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Abstract. We present the workflow of the offline-PET based range verification method used at the Heidelberg Ion Beam Therapy Center, detailing the functionalities of an in-house developed software application, SimInterface14, with which range analysis is performed. Moreover, we introduce the design of a decision support system assessing uncertainties and facilitating physicians in decisions making for plan adaptation.

1. Introduction
Due to the favourable physical properties of charged particles, ion-beam therapy is able to achieve highly conformal energy deposition in the target volume while better sparing surrounding tissue. Yet the superior conformity requires high precision of treatment delivery. Various in-vivo range verification methods have been proposed to monitor dose delivery in particle therapy [1]. Among these, positron emission tomography (PET)-based verification is being investigated clinically at the Heidelberg Ion Beam Therapy Center (HIT) [2]. The evaluation is performed by an in-house developed MeVisLab software application SimInterface14, with which range analysis is performed. Moreover, we introduce the design of a decision support system assessing uncertainties and facilitating physicians in decisions making for plan adaptation.

2. Materials and Methods
At HIT patient plans with scanned proton and carbon ion beams are optimized by the SIEMENS SyngoPT treatment planning system. Selected patients undergo PET imaging with a SIEMENS Biograph mCT full-ring PET/CT scanner for 30 minutes shortly after their treatment fraction. As the
measured spatial activity distribution is not directly proportional to the dose distribution, the evaluation
is based on a comparison between the measured and predicted activity distribution. The prediction is
obtained from a detailed Monte-Carlo simulation and wash-out model [3]. For each patient under
investigation, Monte-Carlo simulation of the expected activity distribution is performed on the treatment
plan via the interface of SimInterface14 to the remote computational cluster, using the automated
framework based on the Monte-Carlo code FLUKA described in [2]. The resulting isotope distributions
are loaded into this MeVisLab application and a wash-out model is applied. This tissue-dependent model
takes patient transferring time (from the treatment room to the PET/CT room) and data acquisition
period into consideration [3]. The decayed signals from different irradiation-induced isotopes are
summed up to obtain the simulated PET image. A Gaussian filter is applied to smooth the image and to
mimic the finite resolution of the PET scanner.

The comparison between the acquired PET and simulated PET is carried out with SimInterface14.
There are two modes for analysis – single spot and beam’s eye view (BEV) evaluation. In single spot
evaluation, profiles are extracted from both acquired and simulated PET images along the beam
direction at a given spot within the BEV. The distal fallofs of the PET signal profiles are identified, and
range shifts are estimated with the forward-zero-padding (FZP) method [5]. Furthermore, as the
alignment of the acquired and simulated PET images are based on registration between treatment
planning CT and PET/CT, the precision of registration affects range shift estimation. To address
registration uncertainties, profiles are also extracted from the planning CT and PET/CT at the same spot
and shift estimation is conducted. An example with a head patient is shown in Figure 1. In BEV
evaluation, firstly a region of interest (RoI) is defined based on the planning target volume (PTV)
projection to the BEV plane with user-set dilation or erosion modification of the boundaries. Then single
spot evaluation is performed for each spot within the RoI. The resulting shift estimation is presented in
a 2D map, as shown in Figure 2. Statistic information, such as mean, variance and standard deviation,
etc. of CT and PET images is gathered for further analysis.

Figure 1. Top panel - A head patient’s
PET/CT image overlaid with measured
PET (right) and the treatment planning CT
overlaid with simulated PET (left) image;
Bottom panel - Shift estimation for a single
beam direction in beam’s eye view (BEV).
The profiles are displayed overlaying each
other (left). Sum of absolute differences
(SAD) are calculated at each shift step,
resulting in a criteria curve (right). The
estimated shift is the one which gives the
smallest SAD in the curve.
3. Results
More than 2000 patients have been treated up to now at HIT. Among them, over 200 patients have been imaged with PET after their treatments for monitoring. The indications of these patients represent the full therapeutic spectrum of HIT. Systematic analysis has been performed for 20 glioma patients, and the mean range shifts were between 2 mm and 4 mm [6]. Moreover, considering range verification for moving target, a feasibility study of time-resolved (4D) PET/CT has been carried out with liver patients. The results showed improvements in range analysis with 4D-PET/CT for targets with superior-inferior motions larger than 10 mm [7]. Evaluation of range uncertainties of the remaining cases is currently ongoing.

In addition to patient studies with the already implemented functionalities, the development of SimInterface14 continues. The final goal is to develop a decision support system (DSS) which gives suggestions if plan adaptation is needed. Figure 3 shows a schematic drawing of the designed structure of the DSS. The inputs of the system are 2D maps of range shift estimations and statistics information within the RoI. The maps can be generally categorized into 3 types: maps to estimate the range shifts, maps to evaluate the reliability of Monte-Carlo simulated PET, and maps to determine the reliability of the estimated shift. For each map, a threshold is set according to the parameter represented by the map. If the value of a voxel is within the given range, this means that the voxel passes certain criteria and it is assigned with value 1. Otherwise the failed voxels are set to 0. The resulted binary maps are multiplied to each other and the “shift and reliability map” (SRM) is created. Based on the information of SRM, the system can provide insights on the necessity of plan adaptation or replanning. To trace back the uncertainties occurred during the treatment and shift estimation, one only needs to look for the 0 values in the SRM and trace back where the 0 values came from. In this way, large shifts of beam range (true positive) or unreliability in PET simulation and/or shift estimation (false positive) can be likely disentangled.

![Figure 2. Estimated range shifts BEV map (left) and histogram (right) for the clinical example shown in Figure 1.](image)

![Figure 3. A schematic drawing of the decision support system.](image)
4. Conclusions
We present an overview of the implementation and recent progresses of our PET/CT-based range verification application in a clinical setting. The current range verification method and the functionalities of SimInterface14 have been described. Furthermore, we introduce the idea of a decision support system, which is able to interpret the results of PET/CT-based verification and track various sources of uncertainties. The ultimate objective is to provide a reliable statement on the measured beam range, and thus support decision making processes towards adaptive particle therapy.

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