each protocol to detect these deviations from the treatment plan is investigated by comparing the planned and the modified PET image. Several analysis methods are used: line profiles coupled to the field-directions, structural similarity index analysis [1], and gamma index analysis. [2]

Preliminary data shows that a difference in density is best detected by starting the scan directly after the first field. However, shifts perpendicular to the field directions are better detected when the scan is done after the last field, due to the increased activity and counting-rate.

Keywords: Positron Emission Tomography, proton therapy dose delivery verification, scanning protocols

References:

36

CTV-PTV margin reduction using prediction of respiration-induced tumour motion

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Purpose: Adaptive radiotherapy aims to synchronize the treatment beam with the tumour motion. It requires the prediction of respiratory motion which has received much attention for over a decade. The performance of prediction algorithms to the dose delivery to the tumour is evaluated for the first time in terms of CTV-PTV margin.

Methods and Materials: Clinical tumour volume (CTV) is outlined in treatment planning and is aimed to be irradiated with sufficient dose. Owing to uncertainties including respiration-induced motion, a sufficient margin around CTV is defined to form planning target volume (PTV). PTV is irradiated to ensure sufficient dose delivery to CTV, whereas CTV-PTV margin should be minimal to avoid irradiating normal tissues outside CTV. In this work, we adopt tumour control probability (TCP) to quantify sufficient dose delivery using TCP model based on Poisson statistics. The CTV-PTV margin required to yield 90% TCP is evaluated for no prediction (a baseline algorithm that refers to using the control probability (TCP) to quantify sufficient dose delivery using TCP model based on Poisson statistics). The CTV-PTV margin should be minimal to avoid irradiating normal tissues outside CTV. In this work, we adopt tumour control probability (TCP) to quantify sufficient dose delivery using TCP model based on Poisson statistics. The CTV-PTV margin required to yield 90% TCP is evaluated for no prediction (a baseline algorithm that refers to using the current measurement as a look-ahead prediction.) and recently proposed EKF-GPRN prediction algorithm [1] at look-ahead lengths of 92 ms, 384 ms and 576 ms. A large database of 304 three dimensional respiratory motion traces from a group of 31 patients is employed to evaluate algorithms. We assume that a spherical-shaped CTV with a radius of 2.5 mm undergoes 3-D motion along these traces. Algorithms are used to predict the center of CTV and the prediction error is considered as the deviation of the treatment beam from the CTV.

Results: Patient-wise statistics for CTV-PTV margin required to achieve 90% TCP is given for each algorithm in the following table. The values in the parenthesis are percent ratios relative to no prediction. The results show that EKF-GPRN reduces the required CTV-PTV margin to around 20% on average, compared to no prediction across all the look-ahead lengths. It indicates that EKF-GPRN can significantly improve dose conformity and effectively reduce normal tissue exposure.

<table>
<thead>
<tr>
<th>Look-ahead Length</th>
<th>No Prediction (% TCP)</th>
<th>EKF-GPRN (% TCP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>92 ms</td>
<td>0.94 (0.06 (17))</td>
<td>0.36 (0.06 (19))</td>
</tr>
<tr>
<td>384 ms</td>
<td>1.30 (0.27 (21))</td>
<td>0.61 (0.13 (31))</td>
</tr>
<tr>
<td>576 ms</td>
<td>2.96 (0.40 (24))</td>
<td>1.94 (0.24 (31))</td>
</tr>
</tbody>
</table>

Keywords: Radiotherapy, respiratory motion, prediction

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References:

37

Robustness and reliability of PET-based identification and quantification of tumor hypoxia, using simple static or more complex scan acquisitions

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Purpose: Tumor hypoxia is linked to poor prognosis, but personalized hypoxic intervention with radiosensitizers (e.g., nimorazole), bioreductive drugs or dose escalation to hypoxic tumor volumes may improve outcome. Hypoxia-selective PET tracers like FMISO and FAZA are available, but inherent weaknesses of PET in general (low resolution) and hypoxia PET in particular (low image contrast due to slow tracer retention and clearance) may compromise the quantitative accuracy and reproducibility of hypoxia PET.

Methods: To assess the severity of this problem, and refine and optimize scan protocols to overcome them, various human and rodent tumors were established in mice. Subsequently, mice were scanned using different scan protocols on a high-resolution (~1 mm) Mediso nanoPET/MRI. Some mice were scanned dynamically for 3-hours to allow full pharmacokinetic analysis (PET imaging gold standard) followed by tumor dissection, cryosectioning and high-resolution analysis of tracer distribution (autoradiography) and hypoxia (pimonidazole), on multiple tissue sections covering the whole tumor volume. Other mice were scanned stastically at two different post-injection (PI) time points, to mimic the image contrast obtainable clinically (1.5h PI) and a much better contrast (3h PI), which can only be obtained in rodents due to rapid clearance of unbound tracer in organisms with high metabolic rates. On the next day, the same mice were scanned again at 1.5h PI or at 1.5 and 3h PI followed by invasive tissue analysis as described above.

Results/Conclusions: An analysis of the distribution of FAZA (autoradiograms) and hypoxia (pimonidazole) on tissue sections revealed that 3h PI static scans, provide highly accurate spatial information on hypoxia, and thus serve as a gold standard. Despite a dramatic increase in inter-tissue and intra-tumoral image contrast at late scan times (3h PI), a voxel-by-voxel comparison revealed an excellent correlation between early (1.5h) and delayed (3h) scans. In addition, the day-to-day spatial reproducibility (overall tracer uptake and its spatial distribution) was good, even when scans were acquired at a clinical achievable contrast. Taken together, these results suggest that target definition is reasonable robust and reliable at a clinical achievable contrast. In contrast a simplified, and thus clinically feasible, dynamic model that both integrates information on blood flow/tracer wash-in (deduced from the FAZA signal during the first 15 min of the scan) and tracer retention (deduced at 1.5h PI), was unexpectedly less reliable, in terms of hypoxia-specificity, than the uncorrected low-contrast static scan. This may relate to an uncoupling between blood flow and oxygen delivery capacity in the abnormal tumor vasculature. Whether, similar limitations apply to full dynamic scans are currently being investigated, using a variety of differing pharmacokinetic models.

38

Single particle detection for spectroscopic CT and tracking in hadron therapy using Medipix chips

Acknowledgements:

References:
Tracking detectors at the LHC rely on hybrid pixel detectors which tag each particle with an extremely high signal to noise ratio and with a time precision of at most 25ns. The same technology has been adapted to numerous other applications by successive Medipix Collaborations. The most recent imaging chip, called Medipix3, permits spectroscopic X-ray imaging at high spatial resolution and relatively high fluxes by using inter-pixel hit-by-hit processing. The Timepix3 chip, on the other hand, takes the opposite approach detecting each hit with a time precision of 1.6ns and sending all data off chip for analysis. Both chips have opened new applications in the medical field: the first for spectroscopic X-ray imaging and CT and the second for beam and dose monitoring during hadron therapy. The presentation will describe the detection technology and focus on some examples of medical applications.

Keywords: Medipix, tracking detectors, CT, hadron therapy

Development of a PET Insert for Human Brain Imaging: Detection System
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In recent years, the combination of techniques such as PET (Positron Emission Tomography) and MRI (Magnetic Resonance Imaging) has shown a great potential to study the processes and progression of diseases (cancer, Alzheimer’s) as well as to control and observe novel treatments response. A brain-size PET detector ring insert for an MRI system is being developed that, if successful, can be inserted into any existing MRI system to enable simultaneous PET and MRI images of the brain to be acquired without mutual interference.

The PET insert consists of detector blocks arranged in a ring of 30 cm diameter. Each detector block is composed of a LYSO array coupled to the Philips Digital Photon Counting. We divided the study of the detection system in three stages. First, we characterized the coupling of the scintillator crystal with the SiPM (Silicon Photomultiplier). Next, we simulated the behaviour or the ring insert using Monte Carlo methods. Finally, we verified the simulation results with the collected data. As a result of this methodology, we obtained the I-V curves and the energy and time resolution of our system. Results show that the coupling is appropriate and that the sensibility of our system is adequate to move to the next study phase: MRI compatibility.

Keywords: positron emission tomography, PET, PET/MRI, detectors, magnetic resonance imaging

A local and global liver function model
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As the use of SBRT for liver tumors increases and repeated treatments for the same patient become more common, it is increasingly important to predict liver function reserve rather than only likelihood of radiation-induced liver disease after SBRT. This study aimed to develop a local and global function model in the liver based upon regional and organ function measurements to support individualized adaptive RT. This local and global liver function model was constructed with the assumption of parallel architecture in the liver, so that the global function of the organ was composed of the sum of local function of subunits similar to a previous model [1]. A major advance in this model is the addition of incorporation of functional variability of the liver across the patients as well as the function probability variability over the subunits between 0 and 1, instead of being a binary number of 0 or 1. This model was fitted to 59 datasets of liver regional and global organ function measures from 23 patients obtained prior to, during and 1 month after RT. The local function probability of a subunit was modeled by a previously published sigmoid function related to MRI-derived regional portal venous perfusion values. The global function was fitted to an indocyanine green retention rate at 15 min. Cross-validation was performed by leave-m-out tests. Fitting was also performed separately for the patients with hepatocellular carcinoma (HCC) vs all others due to likely differences in the liver function as well as radiation sensitivity.

The fitted liver function model showed that 1) a portal venous perfusion value of 68.6 ml/(100g·min) yielded a local function probability of 0.5; 2) the local function probability reached 0.9 at a perfusion value of 98 ml/(100g·min); and 3) at an average function probability of 0.03 (corresponding perfusion of 38 ml/(100g·min)) or lower, the subunits did not contribute to the global function. Cross-validations showed that the model parameters were stable. Further, the same amount of portal venous perfusion was translated into less local function probability in patients with HCC than without HCC, reflecting the compromised local liver function by cirrhosis (Fig 1). The utility of this liver function model was explored, including assessing for individual regional dose response functions that substantially differed from the population average dose response and for dose re-distribution planning by maximizing global liver function by sparing local highly functional regions. This model could be a valuable tool for individualized treatment planning of RT.

Keywords: liver function model, function reserve, individualized RT

References: