4D treatment (planning) workshop 2013

Paul Scherrer Institut
Switzerland
## 4D treatment (planning) workshop - program

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<tr>
<td>10:00</td>
<td>welcome</td>
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<td>10:30-12:00</td>
<td>1. session</td>
<td>Auditorium</td>
<td>moving targets / clinical overview about indications - what is the state of the art to treat moving targets?</td>
<td>Overview about clinical indications of moving targets - report on state of the art treatment</td>
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<td>12:00-13:30</td>
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<td>13:30-15:00</td>
<td>2. session</td>
<td>Auditorium</td>
<td>4D dosimetry - what is available / what do we still need?</td>
<td>Needs and potential solutions for treatment plan verification in 4D treatments of moving organs</td>
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<td>15:00-16:30</td>
<td>posters &amp; coffee</td>
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<td>16:30-18:00</td>
<td>3. session</td>
<td>WPTA 139</td>
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<td>Pros and cons of fluoroscopy based motion detection</td>
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<td>20:00</td>
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<td>8:30-10:45</td>
<td>4. session</td>
<td>Auditorium</td>
<td>4D treatment planning / different motion mitigation techniques - what is the optimal facility characteristics to treat moving targets?</td>
<td>Overview of motion mitigation techniques - clinical practice versus future vision</td>
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<td>Entrance Auditorium</td>
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<td>4D treatment procedure at GSI</td>
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<td>11:15-12:45</td>
<td>5. session</td>
<td>Auditorium</td>
<td>4D optimization - the ultimate solution?</td>
<td>The optimal 4D treatment plan - which concepts of the 3D world can be applied in the 4D world</td>
<td>Stephen Dowdell</td>
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<td>12:45-13:15</td>
<td>summary</td>
<td>Auditorium</td>
<td>highlights / report / location &amp; focus next year</td>
<td>Advanced 4D Optimization - what is possible and what is practical</td>
<td>Christian Graeff</td>
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<td>13:30-14:30</td>
<td>lunch (optional)</td>
<td>Oase (PSI)</td>
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How to get to PSI:

The main part of the workshop will take place at the auditorium at the entrance gate at the PSI west side. Watch out for the “elephant”.

Example Bus/Train connections to/from Zurich for during the workshop:

28.11. – from PSI to Zuerich
Villigen, PSI West 18:04  BUS 376 Richtung: Brugg
Brugg 18:30  IR 1987 Richtung: Zürich HB
(Ankunft 18:54)

29.11. – from Zuerich to PSI
Zürich HB 07:36  IR 1960 Richtung: Basel
Brugg 08:04  BUS 376 Richtung: Villigen (Ankunft PSI West 8:15)
Fare ChF 10,20 one way
Dinner at the first workshop day:

Dinner is arranged for 20:00 o’clock at a Restaurant called Der Schwiizer (Zwinglistrasse 3, 8004 Zürich, http://www.derschwiizer.com/). It is located within 10min walk from the main station in Zurich.
Poster abstracts:

1. Treatment planning strategies for treatment of pancreatic tumors with scanned carbon ions considering inter-fractional organ motion

Batista V(1), Richter D(3), Jäkel O(2) and Combs S(1)
1 University Clinic of Heidelberg (HIT), Heidelberg, Germany
2 Heidelberg Ion Therapy (HIT, Heidelberg, Germany
3 University Clinic of Erlangen, Erlangen, Germany

Purpose: Definition and evaluation of treatment planning parameters for scanned carbon ions to manage inter-fractional motion uncertainties in treatments of pancreatic tumors.

Background: The anatomic localization of the pancreas as well as motion and deformation of the organ itself over the course of the treatment (studies from photon therapy) can substantially impact scanned carbon ion dose delivery, leading to potential degradation of target coverage, due to inter-fractional range changes and geometric miss.

Materials and methods: This initial study included 10 patients with weekly 3DCT imaging and focused on GTV coverage using CTV margins as a first step to guide the PTV definition. The GTV was delineated for the planning and each follow-up CT. Scanned carbon ion treatment plans were optimized for a dose of 15x3Gy(RBE) to the planning GTV using an isotropic CTV margin of 5mm (Plan0). Six possible beam angle configurations with one or two fields were used (anterior A, posterior P, oblique posterior right OPR, lateral right LR, posterior+lateral right P+LR, oblique posterior right and left OPR+OPL). For each patient and each weekly CT, target coverage and the homogeneity index (HI) of the respective weekly GTV volume were analyzed for irradiation with Plan0.

Preliminary results: HI and target coverage depended considerably on the respective beam geometry and the treatment day. Configurations A and LR in particular exhibited substantial range changes degrading the treatment dose. Quantitatively the changes in GTV coverage were largest for beam configuration A (V95=82.0±8.1%). Best results were obtained for beam geometries with less deformation of the surrounding tissues, i.e., for the single posterior field (V95=98.7±0.8%) and the P+LR configuration (99.2±0.6%). Compared to the planning situation, HI values for configurations A and LR were substantially increased and showed large inter-patient and daily fluctuations of on average 10.3±10.9% (A) and 19.5±25.0% (LR).

Conclusions/Outlook: Selection of adequate beam configurations in carbon ion beam therapy of pancreatic tumors taking into account inter-fractional organ motion is of great importance. Single posterior and oblique posterior right fields may have the potential for acceptable and robust target coverage. Definition of robust ITV and PTV margins based on these results will be subject of further research.
2. A prototype tracking system using the treatment couch

Lang S(1), Zeimet J(1,2), Ochsner G(2), Schmid Daners M(2) and Klöck S(1)

1 Department of Radio-Oncology, University Hospital Zürich, Zürich, Switzerland
2 Institute for Dynamic Systems and Control - ETH, Zurich, Switzerland

Purpose: Tumor motion increases safety margins around the clinical target volume and leads to an increased dose to the surrounding healthy tissue. We have developed and evaluated a treatment couch tracking system to counter steer respiratory tumor motion. Three different motion detection sensors with different lag times were evaluated.

Methods: The couch tracking system consists of a motion detection sensor, which can be the topometrical system Topos, the respiratory gating system RPM or the laser triangulation system and the Protura treatment couch. The control system was implemented in the block diagram environment Simulink. To achieve real time performance the Simulink models were executed on a real time engine, provided by Real-Time Windows Target. To achieve high control performance with good reference tracking and good disturbance rejection, a proportional-integral control system was implemented. The lag time of the couch tracking system using the three different motion detection sensors was determined with a step function of 2 cm on the position reference signal.

The geometrical accuracy of the system was evaluated by measuring the mean absolute deviation from the reference (static position) during motion tracking. A hexapod system was moving according to 7 respiration patterns previously acquired with the RPM system as well as according to a sin6 function with two different frequencies (0.33 Hz and 0.17 Hz) and the treatment table compensated the motion.

Results: A prototype system for treatment couch tracking of respiratory motion was successfully developed. The laser based tracking system with a small lag time of 60 ms could track all respiration patterns. An increase in delay time from 60 ms to 130 ms (RPM based system) resulted in a poor tracking performance for the sin6 pattern (frequency 0.33 Hz). The Topos based tracking system with the largest lag time of 300 ms was only able to track four respiration patterns. For the four patient respiration patterns, which could be tracked by all three systems, a mean absolute deviation of 0.19 mm was achieved using the laser sensor, 0.45 mm using the RPM system and 0.52 mm using the TOPOS system.

Conclusions: Couch tracking with the Protura treatment couch is achievable. To reliably track all possible respiration patterns without prediction filters a short lag time below 100 ms is needed. More scientific work is necessary to extend our prototype to tracking of internal motion.
3. Image-based retrospective 4D MRI

Paganelli C, Summers P, Baroni G, Bellomi M and Riboldi M

Purpose: The use of time-resolved (4D) imaging provides a method to quantify intra-fractional anatomo-pathological changes for radiotherapy treatment planning. Due to the absence of ionizing radiation and increased soft tissue resolution, 4D Magnetic Resonance Imaging (4D MRI) is put forward to represent the ideal technology to study organ motion variations, in contrast to 4D Computed Tomography (4D CT). In conventional approaches, derived from 4D CT, an external surrogate is used to resort the images, causing artifacts in the sorted volumes due to limited accuracy in breathing phase identification. Alternatively, image sorting based on a navigator slice can be used, requiring dedicated interleaved sequences to interpolate the correct motion phase. To address these issues, we propose a technique for image-based retrospective sorting of dynamic MRI.

Methods: Free-breathing, dynamic multislice MRI sequences (Siemens Magnetom Avanto 1.5T, TrueFISP sequence, image resolution: 1.28x1.28x5 mm, acquisition time: 150 msec, 20 slices x 20 frames) were acquired on the liver in six healthy volunteers. Four-dimensional MRI volumes were retrospectively derived for eight respiratory phases using both an external surrogate (i.e. respiratory belt) and an internal surrogate based on the image content. This latter was obtained by computing the mutual information between a reference volume (constructed by stacking slices with closest mutual information) and each frame of the image sequence.

Results: Results showed better performance of the image-based approach with respect to the external surrogate. The root mean square fitting error of the liver profile was quantified as 1.87±0.89/1.58±0.91 mm with the internal surrogate with phase/amplitude sorting, whereas 2.17±1.21/2.21±1.22 mm was achieved with the external surrogate approach.

Conclusions: We present a novel methodology employing dynamic MRI to derive a patient-specific 4D model to describe the organ motion due to breathing for treatment planning purposes. Future work is expected to extend the method to 4D CT resorting.
4. Motion compensated reconstructions in 4D PET-based ion beam treatment verification

Gianoli C(1), Kurz C(1,2), Riboldi M(3,4), Bauer J(1,2), Baroni G(3,4), Debus J(1,2) and Parodi K(1,5)

1 Department of Radiation Oncology, Heidelberg University Hospital
2 Heidelberg Ion Beam Therapy Center
3 Dipartimento di Elettronica, Informazione e Bioingegneria, Politecnico di Milano
4 Bioengineering Unit, National Center for Oncologic Hadrontherapy
5 Division of Medical Physics, Ludwig Maximilian University of Munich

Purpose: This study investigates the effectiveness of two motion compensated reconstruction strategies in 4D PET-based ion beam treatment verification. Due to the extremely low count statistics, the independent reconstruction of 4D sinograms (gated) does not result in clinically meaningful images. Both investigated strategies aim at the reconstruction of a motion compensated image making use of all the acquired raw data.

Materials and Methods: The well known 4D MLEM reconstruction was compared to an innovative motion compensation strategy able to provide motion compensated 4D sinograms. The motion model, basically expressed in the image domain, is translated into sinogram domain according to the image-sinogram correspondence and subsequently applied to the low count statistics 4D sinograms. The motion compensated 4D image derives from the summation of the warped 4D sinograms reconstructed by means of the conventional MLEM algorithm. The advantages and limitations of both strategies were assessed and compared. Phantom activation studies were performed and a preliminary study on patient data was also considered.

Results: In presence of regular and rigid motion (Figure 1) the two motion compensated reconstruction strategies demonstrated similar performance (Figure 2 and Figure 3). The advantages of the innovative strategy were investigated on patient data, where the motion model was characterized by 4D CT artifacts and lack of exact 4D CT-PET co-registration (also due to different 4D CT-PET sampling).

Conclusions: Initial results support the effectiveness of motion compensated reconstruction strategies in 4D PET-based ion beam treatment verification for moving targets. The advantages of the new proposed strategy will be further evaluated in an envisioned clinical evaluation.

This work is being supported by ENVISION EU FP7 program.
The 4D CT are interpolated on the spatial and temporal grids of the 4D PET, according to the specific motion function \( \cos^4 \) for the reported phantom. The motion is measured by means of image registration.

**Figure 1.** The 4D CT are interpolated on the spatial and temporal grids of the 4D PET, according to the specific motion function \( \cos^4 \) for the reported phantom. The motion is measured by means of image registration.

**Figure 2.** Comparison between the two motion compensated reconstruction strategies on the phantom acquisition. The 4D motion phases refer to the motion curve reported in Figure 1. **Upper panel:** the 3D PET and the 4D PET phases corresponding to the inhale and exhale peaks. **Central panel:** the 4D MLEM reconstruction strategy. **Lower panel:** the MLEM reconstruction obtained in combination with the sinogram warping strategy.

**Figure 3.** Comparison between the two motion compensated reconstruction strategies on the phantom acquisition (0% motion phase). The 4D motion phases refer to the motion curve reported in Figure 1. The sinogram warping strategy is referred as “4D SW MLEM”.
5. Development of a dynamic phantom for quality control in 4D radiotherapy

Miyamoto N(1), Hirata Y(1), Suzuki R(1), Toramatsu C(1), Kozuka T(1), Miyabe Y(2), Kaneko S(2), Nishio T(3), Shimizu S(1), Ishikawa M(1) and Shirato H(1)

1 Graduate School of Medicine, Hokkaido University, 060-8638 Sapporo, Japan
2 Graduate School of Medicine, Kyoto University, 606-8507 Kyoto, Japan
3 National Cancer Center Hospital East, 277-8577 Chiba, Japan

Introduction: A dynamic phantom that can reproduce respiratory motion is essential for acceptance tests, commissioning tests, and routine quality control in 4DRT systems. In order to gather the data for the verification efficiently, we have developed a dynamic phantom that has an input/output signal port in order to synchronize with a 4DRT system. In addition, it has high positioning accuracy compared with ordinary commercial devices. The developed dynamic phantom was used for commissioning tests. In this study, the usefulness of the dynamic phantom is reported, showing the results of commissioning tests.

Methods and Materials: A respiratory-gated radiotherapy system utilizing dual fluoroscopy was commissioned. In this 4DRT system, two fluoroscopy devices are utilized to measure the 3D location of fiducial markers during treatment. The dynamic phantom was used to imitate respiratory motion of the marker. Measurement accuracy of the moving marker can be evaluated by comparing the log of the controlled marker position by the dynamic phantom and the log of measured marker position by the imaging system. Motion and data logging of the dynamic phantom are initiated by the first signal of fluoroscopy by using the input/output port. In this way, data logging of each system was synchronized easily. The 4D dose distribution was confirmed with radiochromic films.

Results and Conclusion: The measurement accuracy of the fiducial marker, which was within 1 mm, could be evaluated with a simple procedure by using the input/output port. Flatness, symmetry and penumbra of the 4D dose were examined precisely in various conditions. These characteristics will be necessary to determine target margins. The developed dynamic phantom was applicable for quality control in 4DRT. By using the input/output port, verification of more complex situations, such as baseline-shift or variation of respiratory cycle/amplitude during irradiation, can be performed.
6. Evaluation of the measurement accuracy of a novel monoscopic x-ray imaging system for real-time tumor-tracking radiotherapy

Miyamoto N(1), Ishikawa M(1), Sutherland K(1), Suzuki R(1), Matsuura T(1), Takao S(1), Toramatsu C(1), Nihongi H(1), Shimizu S(1), Umegaki K(2) and Shirato H(1)

1 Graduate School of Medicine, Hokkaido University, 060-8638 Sapporo, Japan
2 Graduate School of Engineering Hokkaido University, 060-8638 Sapporo, Japan

Introduction: In the current real-time tumor-tracking radiotherapy (RTRT) system, respiratory motion of the internal fiducial marker is monitored by two fluoroscopy systems during treatment. In this study, a novel RTRT system with a monoscopic x-ray imaging system is proposed. Measurement error of the proposed approach was analytically examined and is reported.

Methods and Materials: In RTRT for lung, multiple fiducial markers are usually implanted near the tumor. In case that the distances between the markers are known, the 3D location of each marker can be measured from a single image without any prediction based on statistics and/or probability. Measurement error of the 3D marker location depends on alignment of multiple markers and 2D registration error of the fiducial markers in the fluoroscopic image. Measurement error was defined as the difference of the actual 3D location of the fiducial marker and the measured 3D location by assuming the image registration error of the marker. For the first evaluation, the 2D image registration error was assumed to be 0.1 mm. This registration error can be realized by means of a sub-pixel registration technique. The actual dispositions of three fiducial markers of 68 RTRT plans were used in this analysis.

Results and Conclusion: 3D measurement error less than 2.0 mm was obtained in 35 cases. Measurement error along the imaging-axis was larger than other directions. The reason for the difference of measurement accuracy in each axis was that the variation of the marker location along the imaging-axis gives small variation of the projected marker position compared with other axes. The proposed approach had acceptable measurement error, 2.0 mm in this study, in about half the cases. In addition, it was found that the measurement error was reduced by changing the imaging direction. Optimization of the imaging geometry will be our next task.
7. Comparison of PTV concepts for lung cancer patients with scanned proton beams

Jakobi A, Knopf A, Perrin R and Richter C

The impact of different planning target volume (PTV) concepts in lung cancer proton therapy on the dose coverage of the tumour volume was analyzed for five patients.

At Dresden University Hospital (UKD) patient treatment with an IBA proton therapy gantry will be started in 2014. The IBA gantry nozzle is capable of delivering protons by scattered beam and scanning beam technique (universal nozzle). As shown in previous work, for static cases the scanning technique is capable to deliver a more conformal dose distribution to the patient. Anyhow, in the presence of motion that conclusion could be incorrect.

This project aims on identifying the optimal lung cancer treatment technique for proton facilities using the IBA gantry specifications. Therefore realistic dose distributions need to be considered that incorporate motion e.g. by the means of 4D-CT and patient specific respiration patterns.

First calculations were done for the active scanning treatment technique. Since the margin concept highly influences the motion impact, three different strategies used in literature are evaluated. All three are based on a planning target volume (PTV) that is derived from an internal target volume (ITV) delineated by a physician based on the gross tumour volumes of eight 4D-CT phases: (1) PTV as target with overwritten Hounsfield Units in the PTV, (2) PTV as target with overwritten Hounsfield Units in the ITV, (3) Beam-specific PTVs incorporating the uncertainties due to density changes in the beam path caused by motion. For a small number of patients it could be shown that the beam specific PTV is superior in patients with large tumour motion. For patients with small tumour motion (< 0.5 cm) all three concepts lead to similar tumour coverage. For a general conclusion, this finding needs to be validated on a larger patient cohort.
8. Four-dimensional dose calculation in dynamic tumor tracking irradiation using the gimbaled x-ray head of Vero4DRT

Miyabe Y(1), Nakamura M(1), Ishihara Y(1), Nakamura A(1), Matsuo Y(1), Itasaka S(1), Monzen H(1), Mizowaki T(1), Kokubo M(2) and Hiraoka M(1)

1 Department of Radiation Oncology and Image-applied Therapy, Graduate School of Medicine, Kyoto University,
2 Department of Radiation Oncology, Kobe City Medical Center General Hospital

Introduction: The Vero4DRT system has the capability for dynamic tumor-tracking (DTT) irradiation using a unique gimbaled X-ray head, and we applied DTT irradiation clinically in lung, liver and pancreas cancer patients. For treatment planning and evaluation of 4D dose distribution, we developed the 4D dose calculation system and estimated its accuracy. The commissioning results are reported in this paper.

Materials and Methods: The 4D dose distribution was calculated using 4D-CT and deformable image registration (DIR) technique. Dose calculation was performed on each respiratory phase 3D-CT image set using an in-house developed Monte Carlo (MC) system which can simulate swing motion of gimbaled x-ray head. The calculated dose distribution was mapped to the reference 3D-CT image through the DIR, and the 4D dose was obtained by summing the mapped doses. The DIR and dose mapping were performed using commercial software MIM Maestro.

The accuracy of the MC dose calculation was verified with ion-chamber and film measurements in static and moving phantom. The geometric accuracy of DIR was evaluated on 15 patients (10 cases of lung cancer, 2 cases of liver cancer and 3 cases of pancreas cancer). Deformation vector fields (DVFs) from inhale CT to exhale CT images were computed for each data. The calculated DVFs for anatomical landmarks, such as lung vessel bifurcations and VISICOIL fiducial marker in liver and pancreas, were compared with the manually measured displacements.

Results: The average difference between the MC simulated and measured doses were within 2.0% for stereotactic fields in any gimbal rotation angles. For IMRT fields with DTT, the average differences were within 3.0%. The average accuracy of DIR for lung cancer patients, as determined via landmark analysis, was 1.4+/-1.4 mm. On the other hand, DIR algorithm produced deformation fields with physically unrealistic aspects in the liver, and large positional error (maximum 9.9 mm) was observed.

Conclusions: The developed 4D dose calculation system showed acceptable accuracy in lung cases. However, large deformation errors can occur especially within homogeneous region. DIR performance on each patient should be assessed before clinical application.
9. Realization of intensity-modulated dynamic tumor-tracking radiotherapy with real-time monitoring using the gimbaled x-ray head of Vero4DRT

Nakamura M(1), Miyabe Y(1), Ishihara Y(1), Nakamura A(1), Matsuo Y(1), Itasaka S(1), Monzen H(1), Mizowaki T(1), Kokubo M(2) and Hiraoka M(1)

1 Department of Radiation Oncology and Image-applied Therapy, Graduate School of Medicine, Kyoto University,
2 Department of Radiation Oncology, Kobe City Medical Center General Hospital

We started performing intensity-modulated dynamic tumor-tracking radiotherapy (IM-DTRT) using the gimbaled x-ray head of the Vero4DRT for three pancreatic cancer patients in June 2013. This study presents a treatment procedure for IM-DTRT using the gimbaled x-ray head of the Vero4DRT. One Visicoil fiducial marker was implanted percutaneously within or near the tumor 1~2 weeks before the 4DCT scan. In preparation, all patients were immobilized on a BodyFix vacuum cushion with both arms raised. Then, 4DCT scan was done under free breathing using the Varian Real-Time Position Management System with a slice thickness of 2.5 mm in axial cine mode. The 4DCT datasets, consisting of 3DCT datasets for each of ten equally spaced phases of the respiratory cycle, were obtained. Based on 3DCT dataset at mid-respiratory phase, the other nine 3DCT datasets were rigidly superimposed focusing around the Visicoil. The overlaid outlines of the target and OARs were contoured on the 3DCT dataset at mid-respiratory phase. The tracking margin included a correlation model errors, intrafractional errors due to baseline drift, mechanical response errors, and interfractional errors due to displacement of the Visicoil. Six-field step-and-shoot IMRT plans were created. Prescribed doses of 45 to 48 Gy were specified to PTV boost D95 in 15 fractions. A 4D dose evaluation was performed using software developed in-house. After treatment planning approval, dosimetric quality assurance was performed under real respiratory patterns using a four-axis moving phantom that reproduced the 3D target and 1D IR marker motions. Compared to the dose distributions under stationary conditions, the $\gamma$ passing rate was more than 93.7% with the criterion of 3%/3 mm. A 6-MV photon IM beam was delivered to the target with the gimbaled x-ray head toward predicted position based on the abdominal wall motion and a pre-built correlation model. During IM beam delivery, the Visicoil was monitored with kV and MV x-ray imagers. The 95th percentiles of the intrafraction prediction errors were within 3 mm. The mean in-room time was around 23 minutes. In conclusion, IM-DTRT was successfully implemented for pancreatic cancer with the high accuracy and reasonable treatment times.
10. Performance of layered and volumetric rescanning for different scanning speeds of proton beam

Bernatowicz K(1,2), Lomax A(1,2) and Knopf A(1,2)

1 Department of Physics, ETH Zurich, 8092 Zurich, Switzerland.
2 Proton Therapy Center, Paul Scherrer Institute, 5232 Villigen PSI, Switzerland.

Purpose: The principle of rescanning using actively scanned proton beams has been recognized as potentially beneficial for mitigation of motion interplay effects. In this study, we compare layered and volumetric rescanning techniques for four realistic proton delivery designs exhibiting different Beam Position Adjustment Times (BPATs).

Materials and Methods: Volumetric and layered rescanning were compared for four different scenarios - a combination of fast and slow BPATs laterally (4ms & 10ms) and in depth (80ms & 1s); and 9 different treatment plan arrangements for two clinical liver cases with varying tumor size i.e. clinical target volume (CTV) of 98 and 264 cm³. 4D dose calculations were performed using regular, sinusoidal rigid motion assumed as the worst-case motion scenario to model interplay effects. Calculations were sampled over 3 different starting phases resulting in a total of 432 dose distributions. Effectiveness of rescanning was quantified in terms of dose homogeneity (D5-D95 values) and mean dose to CTV. Additionally, treatment delivery time were compared.

Results: For slow scanning systems, D5-D95 values were lower by up to 16% with layered rescanning and the estimated treatment delivery time was reduced by up to 300s. Analysis of dose homogeneity showed that layered rescanning leads to a smoother decrease in dose inhomogeneity as a function of the number of rescans than volumetric rescanning, which shows larger fluctuations. However, layered rescanning appears to be more sensitive to the starting phase. When analyzing the performance of both approaches and different scanning speeds as a function of delivery time, layered rescanning appears to be the only viable approach for systems with a slow energy changes, even approaching the performance of faster systems, as long as lateral scanning speeds are kept high. Similar results were found for multiple field plans and when analyzing different field directions.

Conclusions: In summary, there might not be a dedicated best design for the treatment of moving targets, instead it seems to be important to choose an adequate rescanning technique for a specific proton delivery system design. Our work suggests layered rescanning, as the method of choice for slow scanning systems, both in terms of dose homogeneity and treatment delivery time.
11. The Effect of dose-delivery time structure on biological effectiveness for charged particle therapy

Inaniwa T, Suzuki M, Furukawa T, Mori S, Kanematsu N, Shirai T and Hawkins R B

Treatment plans of c-ion radiotherapy have been made on the assumption that the beams in one fraction are delivered instantaneously by neglecting the dose delivery time as well as the interruption time. However, in practical treatments, it takes 1-10 minutes or longer to deliver a fractional dose to a patient depending on the prescribed dose level, the dose delivery technique and the performance of the delivery system. Especially, the advanced therapeutic techniques such as a hypo-fractionation and a respiratory gating usually require more time to deliver a fractional dose than the conventional one. In addition, the dose delivery can be interrupted due to some reasons such as the necessity of a patient re-setup between fields in a treatment fraction and machine troubles. Cell killing tends to decrease with the fraction time because of sublethal damage repair (SLDR). Thus, it is important to investigate the quantity of SLDR during the fraction time and to evaluate the effects of dose-delivery time structure on the biological effectiveness of therapeutic c-ion beams. In this study, the Microdosimetric Kinetic Model (MKM) was adopted to address this issue.
12. Amplitude-based gated phase-controlled rescanning in carbon-ion scanning beam treatment planning under irregular breathing conditions using lung and liver 4DCTs

Mori S, Inaniwa T, Furukawa T, Takahashi W, Nakajima M, Shirai T, Noda K, Yasuda S and Yamamoto N

Purpose: Amplitude-based gating aids treatment planning in scanned particle therapy, because it provides better control of uncertainty with the gate window. We evaluated the effects of this gating under realistic organ motion conditions using 4DCT data of lung and liver tumors.

Methods and Materials: 4DCT imaging was done for 24 lung and liver patients using the area-detector CT. We calculated the field-specific target volume (FTV) for the gating window, which was defined for a single respiratory cycle. Prescribed doses of 48 Gy(RBE)/1fr/4fields and 45 Gy(RBE)/2fr/2fields were delivered to the FTVs for lung and liver treatments, respectively. Dose distributions were calculated for the repeated 1st respiratory cycle (planning dose) and the whole respiratory data (treatment dose). We applied eight phase-controlled rescannings with the amplitude-based gating.

Results: For the lung cases, CTV-D95 of the treatment dose (= 96.0±1.0 %) was almost the same as that of the planning dose (= 96.6±0.9 %). CTV-Dmax/Dmin of the treatment dose (= 104.5±2.2 %/89.4±2.6 %) was slightly increased over that of the planning dose (= 102.1±1.0 %/89.8±2.5 %) due to hot spots. For the liver cases, CTV-D95 of the treatment dose (= 97.6±0.5 %) was decreased by approximately 1 % when compared with the planning dose (= 98.5±0.4 %). CTV-Dmax/Dmin of the treatment dose was degraded by 3.0 %/0.4 % compared to the planning dose. Average treatment times were extended by 46.5 s and 65.9 s from those of the planning dose for lung and liver cases, respectively.

Conclusions: As with regular respiratory patterns, amplitude-based gated multiple phase-controlled rescanning preserves target coverage to a moving target under irregular respiratory patterns.
13. A realistic, breathing phantom of the thorax for development and testing of new motion mitigation techniques with scanning proton therapy

Perrin R(1), Peroni M(1), Žáková M(1), Schätti A(1), Knopf A(1), Safai S(1), Meer D(1), Zhang Y(1), Lomax T(1) and Parkel T(2)

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The second prototype of the jointly-developed PSI-CSEM phantom has been delivered and is undergoing performance testing. Scanned proton delivery methods will be tested for their motion mitigation capability. These techniques will include fast-rescanning, gated and breath-hold proton therapy in spot and line scanning delivery modes. Here, we describe the phantom and show our first results of the phantom’s performance tests.

The phantom is similar to the first prototype including a close representation of the human thorax: density-matched ribs, sternum, heart, vertebrae and inflatable lungs, with a moving cylinder containing tumour-sized spheres. Breathing motion is pneumatically controlled, and the pressure wave transmitted from a ventilator expands the chest surface while moving the tumour, predominantly in the cranio-caudal direction. Dosimetry is performed with GafChromic films inserted into the tumour.

Some modifications have been made based on our experience with the first prototype. Firstly, a custom-made ventilator was manufactured. Labview controlling software was implemented by CSEM in order to facilitate full flexibility of breathing motion types. It can now perform breathing based on recorded patient respiratory breath flow. Improvements to the geometry to better match a human patient include two skin coverings modelled on male and female surface anatomy. Three insertable lungs are now available with different sized tumours and one designed with deformable MRI-CT registration.

Testing is ongoing to assess i. maximum tumour excursion, ii. trajectory repeatability, iii. correlation of surface and tumour motions, iv. breath-hold reproducibility. We perform these tests using our Beam’s Eye View fluoroscopy system, 4D CT and a distance sensor monitoring the tumour cylinder.

First testing showed that the pressure could be finely tuned to generate sin, sin4, breathhold and patient-specific pressure waveforms in the lungs. Maximum excursion of the tumour under the maximum-recommended pressure ranges was 14 mm and 12 mm for the lungs with large and small tumour inserts respectively. As this did not fit with our specifications (maximum excursion, 20 mm) further development of the lung mechanics is ongoing at CSEM in order to produce adequate tumour and surface motion.

Overall, our first experiences with the new design of this breathing phantom were mostly positive, allowing for flexibility in applying respiratory waveforms to a patient-representative geometry.
14. Effects of anatomical changes on intensity modulated proton therapy in NSCLC patients

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Purpose/Objective: Proton therapy could be highly beneficial for locally advanced lung. However, respiratory motion and anatomical changes over the course of treatment make it challenging to deliver the planned dose, as proton beams are highly sensitive to such variations. The purpose of this study was to quantify the effect of inter- and intrafractional anatomical changes in lung cancer patients on the dose delivery of Intensity-Modulated-Proton-Therapy (IMPT).

Method and Material: Eight stage III non-small-cell-lung cancer patients treated previously with Intensity-Modulated Radiotherapy were selected retrospectively. These patients received a lower dose than our standard dose (66Gy) due to organ-at-risk dose constraints. Typically, the primary tumour close to the mediastinum was treated in combination with multiple lymph nodes. We used the research Pinnacle3 (version: 9.1) to create an IMPT plan with a prescription dose of 66Gy. As planning CT, the 4D-CT derived mid-position (motion-compensated) scan was used. A density override to the IGTV was used to improve robustness. Next to the 4D-CT, describing the respiratory motion, daily 3D motion-compensated CBCT scans were acquired to detect long-term anatomical changes. Deformable image registration was applied on the 4D-CT and CBCTs for dose recalculation, comparison and accumulation over the variable patient anatomies.

Results: The D99 reduced up to 4% (respiration) and 6% (anatomical changes) for the primary tumour and 8% (respiration) and 7% (anatomical changes) for the lymph nodes. Hotspots were observed on the OARs, both due to respiratory motion and anatomical changes. However, the sports were still within clinical constraints.

Conclusion: Patient anatomy changes during a fraction. Despite the use of the IGTV, dose variation was observed due to respiratory motions and anatomical changes. Based on this study, we can conclude that classical planning strategies applied for proton therapy are not always adequate in the lung, and that more advanced planning strategies including knowledge of geometrical uncertainties need to be developed.
15. An in silico Comparison of Scanned Carbon Ion vs. SBRT Single Dose Treatment of Metastatic Lung Cancer

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Treatment of extra cranial tumors deposits with photon-based ablative single dose IGRT (SBRT) has been shown to yield local control rates > 80% with acceptable toxicity [1]. Scanned particle therapy (PT) has proven its efficacy for head and neck tumors. Treatment of mobile tumors of the lung is still challenging due to interplay and range changes. We performed an in silico case study comparing SBRT and PT (carbon ions) in 2 patients to investigate potential benefits of PT in radiosurgery.

Patients were actually treated with SBRT. Patient 1 presents with two lesions in close proximity to the spinal cord; while patient 2 has a single centrally-located lesion in the left lung (Figure 1). The actual treatment plans are compared to simulated treatment with PT using TRIp98 [2] on the clinical 4D-CT. Target coverage (24 Gy) and OAR doses are compared. For SBRT we used isotropic 3 mm margins on ITV; for PT we added margins 3 mm laterally and 1 mm in Beam’s eye view on CTV and then computed a range-considering ITV with 2 mm + 2% range margins. Rescanning was used to counter interplay.

Peak to peak tumor motion was 3 mm and 4 mm for the 2 patients, respectively. Dose cuts are shown in Figure 1 and OAR actual and tolerance doses [3] in Table 1. Both therapies provided excellent target coverage and OAR doses within tolerances, except maximal allowed point dose for smaller airways. For patient 1, the dose outside the target could be drastically reduced with PT, completely sparing spine, heart and esophagus. For patient 2, with a simpler plan geometry and larger lesion, the situation is less clear, with lower doses in some OAR, but slightly higher dose in the left lung.

These two specific cases illustrate the potential of PT in shaping the dose outside the target. This advantage varies with patient anatomy and lesion location, so that patients specifically suited for PT might be identified. The clinical relevance of possible further dose escalation or improved NTCP with scanned carbon ion therapy needs to be validated. This study will be expanded to a total of 20 patients, and also the robustness of PT will be further investigated.
Table 1 – Prescribed and planned doses for target and OARs for both patients in SBRT and PT

<table>
<thead>
<tr>
<th>Target</th>
<th>Prescribed Dose</th>
<th>SBRT</th>
<th>PT</th>
<th>SBRT</th>
<th>PT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Volume (%)</td>
<td>Dose (Gy)</td>
<td>Dose (Gy)</td>
<td>Dose (Gy)</td>
<td>Dose (Gy)</td>
</tr>
<tr>
<td>CTV</td>
<td>99</td>
<td>24</td>
<td>24</td>
<td>24.7</td>
<td>24</td>
</tr>
<tr>
<td>OAR</td>
<td>Volume (cc)</td>
<td>Max Point Dose (Gy)</td>
<td>Volume Max (Gy)</td>
<td>Max Point Dose (Gy)</td>
<td>Volume Max (Gy)</td>
</tr>
<tr>
<td>Heart</td>
<td>&lt; 15</td>
<td>16</td>
<td>22</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>&lt; 0.35</td>
<td>10</td>
<td>14</td>
<td>8.4</td>
<td>9.8</td>
</tr>
<tr>
<td>Smaller Airways</td>
<td>&lt; 0.5</td>
<td>12.4</td>
<td>13.3</td>
<td>11.3</td>
<td>22.8</td>
</tr>
<tr>
<td>Esophagus</td>
<td>&lt; 5</td>
<td>11.9</td>
<td>15.4</td>
<td>6.8</td>
<td>11.1</td>
</tr>
<tr>
<td>Liver</td>
<td>700</td>
<td>9.1</td>
<td>N/A</td>
<td>0.6</td>
<td>20.5</td>
</tr>
<tr>
<td>Lung (Left)</td>
<td>1500</td>
<td>7</td>
<td>N/A</td>
<td>&lt;0.1</td>
<td>25.9</td>
</tr>
<tr>
<td>Lung (Right)</td>
<td>1500</td>
<td>7</td>
<td>N/A</td>
<td>0.2</td>
<td>26.2</td>
</tr>
</tbody>
</table>

Figure 1: Dose cuts of Patient 1 (top) and 2 (bottom), with SBRT left and PT right.

References


16. Shortening IMPT treatment times by reducing proton energy layers

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Purpose: The purpose of this work is to make IMPT treatments faster by reducing the number of energy layers in the treatment plan.

Methods: Our in-house developed multi-criteria treatment planning system ‘Erasmus iCycle’, which features the pencil-beam resampling technique in addition to traditional regular grid pencil-beam placement, was extended with a method to reduce the number of energy layers. The method consists of two components: 1) the iterative exclusion of low-weighted energy layers while constraining previously obtained dose parameters and 2) the inclusion of the number of energy layers in the optimization problem by minimizing the logarithm of the cumulative beam weight per energy layer. The use of the logarithm guides the optimizer to minimizing the contribution of the low-weighted energy layers. Using data of five head-and-neck cancer patients, two IMPT treatment plans were generated for each patient: 1) a ‘standard clinical plan’ using regular grid planning and no energy layer reduction, and 2) a ‘time-efficient treatment plan’ using pencil beam resampling and the energy layer reduction method described above. Both plans of each patient had equal plan quality in terms of the plan parameters considered, as the dose parameters of the standard plan were used as input for the time-efficient plan. We evaluated the number of energy layers in the treatment plans and their expected treatment time per fraction. For the latter we assumed 30 s per beam direction (beam setup), 5 s or 2 s per energy layer, 15 ms per spot and 200 Gp per minute.

Results: The average number of energy layers (over all beam directions) was reduced by 54% (range: 42%-65%) from 132 to 61 when comparing the time-efficient treatment plans with the standard clinical plans, while plan parameters were equal or better in the time-efficient treatment plans. Expected treatment times were reduced by 45% (range: 35%-54%) from 13.7 to 7.6 min on average when assuming 5 s energy switching time and by 36% (range: 28%-43%) from 7.1 to 4.6 min on average when assuming 2 s energy switching time.

Conclusions: This work demonstrates that the treatment time of IMPT can be reduced substantially without loss of plan quality. Implementation of the proposed method will improve IMPT treatment accuracy as shorter delivery times are likely to reduce the effect of intra-fraction motion.
17. Motion analysis for stereotactic radiation therapy of bronchial carcinoma using deep expiration breath hold technique

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Purpose: At the University Clinic in Erlangen, patients with lung tumors are treated with stereotactic radiotherapy in combination with a deep expiration breath hold technique. The aim of this study was to analyze external motion parameters, such as breathing period and amplitude, as well as residual motion during the breath holding phases.

Material & Methods: Retrospective data of 20 patients treated for bronchial carcinoma with 6 MV photon beams and a radiation therapy protocol of 12 x 6 Gy were analyzed for this investigation. Patient positioning was verified by the ExacTrac 5.5.2 X-ray system (ETX) from the BrainLAB AG (Feldkirchen, Germany). This system matches two daily X-ray images to a digitally reconstructed radiograph (DRR) of the planning CT. Additionally, ETX enables an optoelectronic motion tracking function by implementing stereo infrared cameras and reflecting body markers. These markers were located close to the diaphragm in each fraction to measure the external motion as a surrogate. The beam status signal was provided by the Geiger counter GM-10 from Black Cat Systems (Westminster, MD USA), controlled by a LabVIEW (National Instruments, Austin, TX USA) program. The analysis was mainly focused on the respiratory waveform, which was automatically detected according to Lu et. al, 2006 [1]. Amplitudes were determined separately for the free breathing and the breath holding phases of each treatment field. Baseline drifts were estimated after linear regression of the minima and maxima.

Results: The motion surrogate data show a high variation in the breath hold phases. Within the group of 20 patients the mean expiration states are spread over 0.6 to 9.3 mm with mean amplitudes of 6.9 ± 0.2 to 16.7 ± 1.2 mm. Breathing periods are in a range of 2.6 ± 0.6 to 6.8 ± 2.0 s. Baseline drifts are mostly negligible.

Conclusion: The use of deep expiration breath hold technique leads to smaller target volumes but it has to be applied carefully. In the analyzed patients with bronchial carcinoma, the external motion surrogate varied substantially within the treatment course. The correlation between the external and relevant internal motion, has to be further investigated.

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18. Respiratory Motion Estimation, Modelling, and Motion Compensated Image Reconstruction

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Respiratory motion models have been proposed for a wide range of applications in Radiotherapy and other fields. These include planning and guiding treatment and performing motion compensated image reconstruction for e.g. CBCT, PET, and MR. Correspondence (or correlation) models relate the motion of the internal anatomy, which is difficult to directly measure during image acquisition or treatment delivery, to an easily acquired respiratory surrogate signal(s) such as spirometry or the motion of the skin surface. Traditionally the models have been built in 2 steps: 1) determine the motion from some prior imaging data, e.g. using image registration, 2) fit a correspondence model relating the motion to one or more respiratory surrogate signals. The model can then be used to estimate the unknown motion from the surrogate signal(s), and the motion estimates used for motion compensated image reconstruction or for planning and guiding RT.

We have developed a generalised framework for combining the motion estimation (via image registration) and model fitting steps into a single optimisation. Not only does this give a more theoretically efficient and robust approach to determining and modelling the motion, but it also enables the use of ‘partial’ imaging data such as unsorted 4DCT, CBCT projections, or individual MR slices, where it is not possible to determine the full 3D motion from a single image. We have also extended this framework to incorporate motion compensated image reconstruction by iterating between model fitting and image reconstruction. This means it is possible to estimate both the motion and the motion compensated reconstruction just from the partial imaging data (and a respiratory surrogate signal).

We have used a simple 2D ‘lung-like’ software phantom to demonstrate a proof of principle of our framework. We have done this for both simulated projections and ‘thick-slice’ data (representing CBCT and MR data respectively), and a simple diffusion/demons like registration algorithm implemented in matlab. We are now in the process of implementing this framework with our open-source B-spline based registration software, NiftyReg, and testing it on real clinical data.
19. Motion Compensated Dose Reconstruction Option for the Vero SBRT System in Pinnacle3

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Introduction: The Vero system from BrainLAB and Mitsubishi Heavy Industries is a fairly new treatment option for extracranial stereotactic treatments [1]. Based on dedicated imaging systems within the BrainLAB ExacTrac module, monitoring of intra-fractional tumor motion is achieved. The monitoring information is used to adjust the photon beam in real-time to compensate lateral motion with respect to the beam’s eye view. Treatment planning, however, is currently performed in 3D using margins that might be derived patient-specifically from a 4D Computed Tomography (CT) of the patient [2]. Hence, the moving structures are not considered exclusively in the treatment plan optimization as well as in the dose estimation. For the 4D dose evaluation, we propose a method to reconstruct 4D patient dose distribution by implementing a dedicated plugin that is incorporated in a non-clinical research version of the Pinnacle3 treatment planning system.

Materials and Methods: The information of the delivered MU and the linac head geometry (e.g., position of gimbal, MLCs, gantry) versus time is provided by Vero’s machine log. Together with the 4D-CT datasets and the motion pattern that is given by infrared markers during the treatment, that information will be used in a Pinnacle3 plugin to recalculate the dose distribution of each motion phase. Using a deformable image registration that is implemented in the plugin, the dose of each motion phase is mapped into the reference phase as used in the treatment plan so that the results can be evaluated.

Preliminary results: The Pinnacle3 plugin to reconstruct the dose for each motion phase is being developed at our clinic. All input parameters as mentioned above are integrated in this dedicated plugin. One of the parameters, i.e., the motion pattern, is taken from the measured infrared markers of the ExacTrac system.

Discussion and outlook: The proposed method employs motion information and the machine’s log to reconstruct the dose distribution in Pinnacle3. Together with the deformable image registration, the reconstructed dose distribution from this method can be compared with the dose distribution from the preceding treatment plan to acquire the dose evaluation. Measurements using a dedicated moving phantom will be used to verify the accuracy of the method. The results of this study will be used to develop an adaptive protocol in Pinnacle3.

Acknowledgment: This work is part of research collaboration with Philips Healthcare. We acknowledge Matthieu Bal and Karl Bzdusek from Philips Radiation Oncology System for their support of this project.
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20. Current Status of 4D Offline PET-Based Treatment Verification at the Heidelberg Ion-Beam Therapy Center

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At the Heidelberg Ion-Beam Therapy Center, patient treatment with protons and heavy ions is monitored by comparing the irradiation-induced β+-activity, measured by a commercial full-ring PET/CT scanner installed next to the treatment room (offline), with a corresponding Monte-Carlo (MC) simulation generated on the basis of the treatment plan and the time-course of irradiation and imaging. While the usefulness of 3D offline PET-based treatment verification has already been shown, the feasibility of 4D offline PET-based treatment monitoring still needs to be demonstrated.

To this aim, an experimental study with PMMA phantoms of different geometries, irradiated once under stationary and once under moving conditions, has been performed. The rigid phantom movement has been monitored by the ANZAI pressure sensor during the gated beam delivery, as well as during the subsequent PET/CT scan. In a similar way, the respiratory motion of several Hepato-Cellular Carcinoma patients has been recorded during their carbon ion irradiation and the post-treatment verification PET scan. In the phantom and in the patient case, this enabled a 4D analysis of the actually applied treatment, resulting in a 4D MC prediction of the induced β+-activity. This prediction has then been compared to the 4D reconstructed PET images and, in the case of the phantoms, to a static reference measurement and simulation.

It could be shown that in the simplified, high-dose scenario of moving phantoms, results comparable to the static reference cases can be achieved, thus proving the feasibility of time-resolved offline PET-based treatment verification. The 4D analysis of clinical data, on the other hand, was found to be hindered by the extremely low counting statistics in combination with the presently available gated 4D PET image reconstruction, which further subdivides the measured coincidences into the different motion phases prior to reconstruction. Still, in the
case of small motion amplitudes (around 1cm), differences in 3D and 4D calculated activity distributions are small, and treatment verification by comparing 3D MC simulation and 3D PET images is possible.

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We are looking forward to a vivid and fruitful workshop!!!

Christoph Bert & Antje Knopf

If you have any questions don’t hesitate to drop us an email: antje-christin.knopf@psi.ch or Christoph.Bert@uk-erlangen.de