

4D Treatment Workshop for Particle Therapy

Delft, 12-13 November 2021

HollandPTC is een zelfstandig centrum voor protonentherapie, wetenschappelijk onderzoek en onderwijs in Delft. Opgericht door Erasmus MC, LUMC en TU Delft.



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Programme

4D Treatment Workshop for Particle Therapy 2021

12 – 13 November 2021

	Fri	day 12 November 2021	Saturday 13 November 2021			
	09:30	Reception		08:30-09:00	Motion management for indications beyond the thorax	
	10:00-10:30	Welcome	Moving to the		region Per Poulsen	
		Mischa Hoogeman, Barbara Knäusl	future	09:00-09:30	Dosimetry in 4D	
Perspective	10:30-11:00	Clinician's perspective on 4D proton therapy	Choir:		Hugo Palmans	
. cropeenre		Marco van Vulpen	Stine Korreman			
Chair: Barbara Knäusl	11:00-11:30	Physicist's perspective on 4D proton therapy		09:30-09:45 9:45-10:00	Q&A on moving to the future Poster Pitch (3 speakers a 3min)	
	11.00-11.50	Mischa Hoogeman		10:00-10:30	Coffee Break	
	11:30-11:45	Q&A on perspective		10:30-11:00	How to stop a tumor that moves with respiration? Nicolas Peguret	
	12:00-13:30	Lunch	Future			
	13:30-13:45	Poster Pitch (3 speakers a 3min)		11:00-12:00	How to get FLASH moving?	
Current status	13:45-14:15	Learning from the MD Anderson experience - how to	Chair: Per Poulsen		Beth Rothwell and Mat Lowe	
		manage moving targets? Thomas J Whitaker		12:00-12:30	How to do daily adaptations in proton therapy?	
Chair: Marco van Vulpen	14:15-14:45	Do we currently see what we treat?			Stine Korreman	
		Chiara Paganelli		12:30-12:45	Q&A on future	
	14:45-15:00	O&A on current status		12.30-12.45	day of future	
	15:00-15:30	Coffee Break		12:45-14:15	Lunch	
				14:15 - 15:15	4D treatment planning: round table discussion	
Debate Chair:	15:30-16:30	MR vs X-ray guided proton therapy - which way to go? Aswin Hoffmann vs Dennis Schaart	Round table		lead: Antje Knopf	
Mischa Hoogeman						
	16:45-19:00	Apero & Posters & Tour		15:15-15:30	Closing remarks - Poster award	
	19:30	Dinner at restaurant 'Het Boterhuis', Markt 15, Delft			-	

Location:

De Oude Bibliotheek Academy Raam 180, 2611 WP Delft Pre-Conference Drinks Thursday 11 November – 20:00h

Pavarotti, Stationsplein 14, Delft



Format of round table discussion

The round table discussion will be held in small break-up groups. The nine topics for discussion are listed below. During the workshop, all participants can sign up for one of the topics. Signing-up will be on a first comes basis, with a maximum of ~8 people per topic. Each group will have one moderator (name listed in brackets) to guide the internal discussion of the topic in the first 45 minutes of the session with the goal to come up with one summarizing statement per group. The summarizing statements will then be shared in the last 15 minutes of the session when all break-up groups reunite at the "main stage".

Topics:

- 1. Adaptive versus robustly optimized treatment approaches Is one more preferable than the other and /or do we need a mix? (Barbara)
- 2. Will or should 4D optimization be required for the treatment of moving targets with particles in the future? (Antje)
- 3. Which of the following topics should get more attention in the context of 4D treatments in the future and why: beam angle optimization, arc therapy, flash treatments, 4D evaluation? (Ilaria, Silvia)
- 4. Will or should MC dose calculations be required for the treatment of moving targets with particles in the future? (Katarzyna)
- 5. Does fractionation already solve the 4D challenges for particle therapy treatments or do we need gating, tracking, 4D optimization, ... in addition? (Petra)
- 6. How much conformity do we need in 4D particle therapy to be "better" than modern photon therapy? (Christian)
- 7. Do we know what we actually deliver when treating moving targets with particle therapy or should we invest more in monitoring actual occurring dose uncertainties? (Jan)
- 8. How can surface imaging help with motion management in the context of 4D particle treatments? (Mischa)
- 9. How to ensure a clinical translation of 4D approaches in particle therapy? (Antoni)

Abstract no 1: Exploring beamline momentum acceptance of a medical gantry to deliver optimized tumour tracking plans

Authors

Giovannelli AC, Safai S, Meer D, Weber DC, Lomax AJ, Fattori G

Background

Tumour tracking is particularly challenging to realise when it comes to proton therapy. The difficulty of assessing anatomical changes reliably enough to offset the treatment settings on-the-fly, while taking into account the finite range of particles, is beyond the current capabilities of beam delivery and image guidance technologies.

Methods

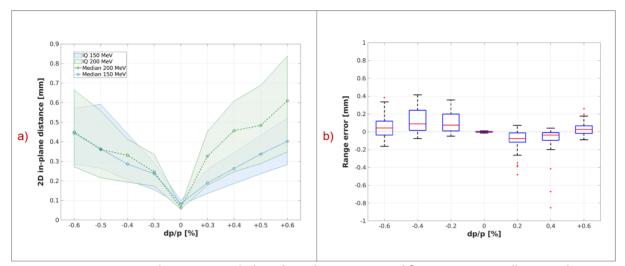
To implement fast range corrections, momentum acceptance (±0.6% dp/p) and global achromaticity of PSI Gantry2 has been exploited. Using a standard upstream degrader, the energy can be modulated around the mean value of the acceptance band without tuning the beamline magnets, overcoming the major source of dead-time in conventional treatments delivery. Being acceptance limited, such ultra-fast energy changes can only be of small magnitude, ~2mm WER. Therefore, at an early stage of planning, 4DCT images of the patient are used to generate a scan-path with dose spots sorted by energy, including tracking offsets, which can synchronized during delivery to the patient motion.

Results

Beam properties within the momentum acceptance of our facility have been characterized between 150 MeV and 230 MeV. Using dedicated correction models for fine range control and compensation of beam intensity losses, a median energy switching time of 27ms could be achieved. Moreover, spot position errors in the transversal plane were below 1 mm across the 18x12 cm scan range.

Conclusions

Rapid adaptation of beam range is essential to deliver tumour tracking plan following patients' breathing. Fast energy modulation can be realized within the beamline acceptance preserving clinical level beam quality.



Beam position errors in the transversal plane have been measured for 35 spots equally spaced on a regular grid covering a 18 by 12 cm scan range. In panel (a), 2D in-plane errors for two energy bands around 150 MeV and 200 MeV are shown at 0.1% steps of momentum. Dashed line is median value and shaded area represents the interquartile range of error for all measured points.

In panel (b) are the beam range errors measured at isocenter for 40 energy bands going from 150 to 229 MeV at 0.2% dp/p momentum steps.

<u>Abstract no 2:</u> Conformal particle therapy of moving tumors with 3D range modulators and proton radiography

Authors

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Background

3D range modulators (3DRM) would enable conformal particle therapy with a single energy and, thereby, ultra-fast treatment delivery. However, accurate dose delivery with 3DRMs requires exact tumor position alignment with the designed 3DRM, making the application to lung tumors challenging. Single-event particle radiography (pRad) could be suitable for generating motion feedback and triggering dose application. Here we investigate the possible treatment benefit achievable with such a setup.

Methods

Prior to treatment irradiation, we assume continuous dynamic acquisition of low-dose pRad to provide motion feedback. The acquired pRads enable to guide the patient to 'breathe' the tumor in position and then hold breath. The irradiation is briefly gated (O(300ms)) to drive the 3DRM into the beam and to adjust beam energy/intensity, and, apply the treatment in a single ultra-fast irradiation (O(100ms)). Lung tumor imaging with single-event proton radiography was investigated in Monte Carlo simulations of an XCAT patient featuring a 5cm diameter tumor in the lower lobe. Assuming ideal feedback from pRad, a quasi-static dose calculation for a 3DRM was conducted with the TRiP98 treatment planning software, and compared to a perfectly rescanned ITV plan for a periodic IS-motion with 20mm amplitude.

Results

pRad allowed to distinguish the tumor from the lung background and enables beams-eye-view monitoring of lateral tumor position and water equivalent thickness. A quasi-static 3DRM treatment reduced mean OAR dose relative to target dose from 16% (lung) and 1% (heart) to 11% and 0.3% compared to an ITV treatment, while keeping target coverage of D95>97%. Especially, heart D15cc was reduced from 12.4% to 0.8%.

Conclusion

Using dynamic pRad to trigger treatment delivery via 3DRMs might enable ultra-fast, highly conformal treatment of lung tumors, and could even pave the way towards lung FLASH particle therapy. While no system yet exists for fast dynamic pRad, ongoing research is promising.

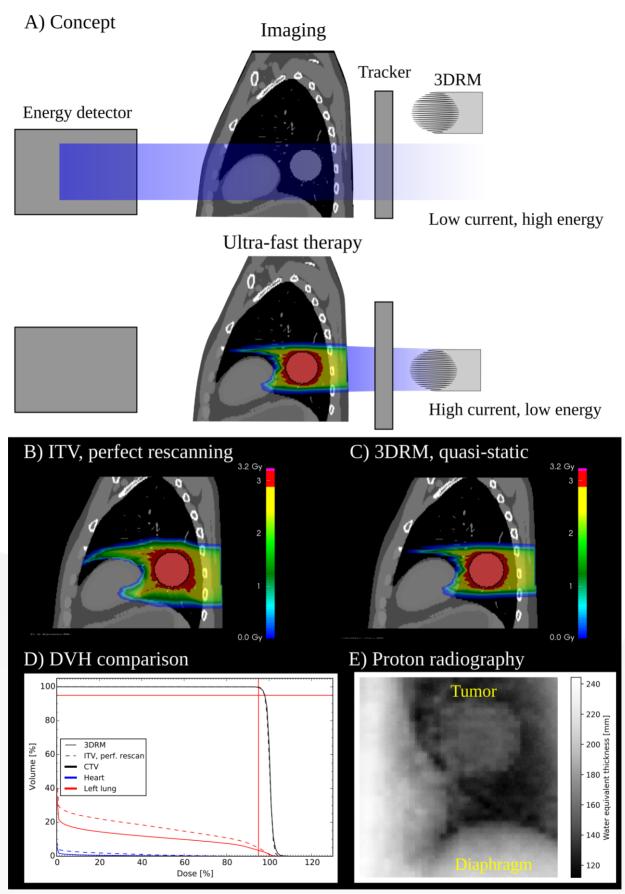


Figure 1: A) Schemtic depiction of the concept. B) Planned dose for an ITV plan, assuming perfect rescanning. C) Dose with a 3DRM, applied quasi static. D) Comparison of DVHs. E) Single-event proton radiograph (5x10⁶ primaries at 230 MeV initial energy) of a 10x10cm² field-of-view including the tumor and diaphragm.

<u>Abstract no 3:</u> Scatter correction of 4D cone beam computed tomography for time-resolved proton dose calculation: first patient application

Authors

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Background

Image-guided adaptive proton therapy addressing inter- and intrafractional changes is expected to have clinical benefits. Time-resolved intensity-modulated proton therapy (IMPT) dose calculations were performed on a planning 4DCT and a day-of-treatment 4D virtual CT (4DvCT) and scatter-corrected 4DCBCT (4DCBCT_{cor}) for a lung cancer patient to demonstrate feasibility.

Methods

Day-of-treatment free-breathing CBCT projections and planning 4DCT images were used as input to a scatter-correction algorithm, previously validated using a porcine lung phantom [1], to generate updated 4DvCT (CT-to-CBCT deformable registration) and 4DCBCT_{cor} (projection-based correction using 4DvCT prior) images. A 3D robust IMPT plan delivering 60 Gy in 30 fractions with a 3-field arrangement was created on a contoured 3D planning CT using a research version of the treatment planning system RayStation. A density override of the 4DCT-derived ITV using muscle tissue was performed. The Monte Carlo dose engine used a statistical error of 1%. Clinical robustness settings of 3% range and 6 mm setup error were applied. Subsequently, the dose was re-computed without density override on every phase and modality (planning 4DCT, day-of-treatment 4DvCT, 4DCBCT_{cor}) as displayed in figure 1. Evaluation of the different methods was performed by comparison of ITV and OAR dose volume histogram parameters on individual motion phases.

Results

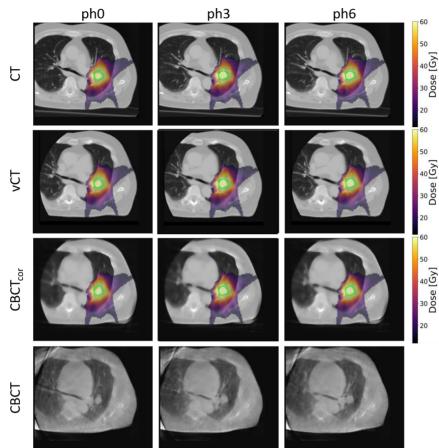
Quality enhancements in 4DvCT and 4DCBCT_{cor} compared to 4DCBCT were observed. Dose values, shown in table 1, deviated by less than 1% between 4DvCT and 4DCBCT_{cor} for left lung mean dose and ITV D₉₈. A maximum deviation of 5% was observed for mean heart dose and in-field bronchi D₂. Larger differences to the 4DCT were expected as the acquisition was on different days.

Conclusions

The results of our study suggest that it is feasible to perform accurate daily time-resolved proton dose calculation for lung tumour patients on 4DvCT and 4DCBCT_{cor}.

Acknowledgements

DFG: 399148265, GRK2274



[1] Schmitz et al., Phys. Med. Biol. (2021), https://doi.org/10.1088/1361-6560/ac16e9

Figure 1: Proton dose distributions for phase 0, 3 and 6 (in total 10 phases were reconstructed) calculated on 4DCT, 4DvCT and 4DCBCT_{cor} overlaid on the images (level = -300 HU and window = 1600 HU). To improve clarity, no values below 15 Gy are shown. The ITV is shown in green. The CT treatment table is not horizontal due to CT to CBCT rigid registration (accounted for at planning). Additionally, the non-corrected 4DCBCT is shown using the same window/level.

Table 1: Dose volume histogram parameters of different regions-of-interest (ROI) for the three images4DCT, 4DvCT and 4DCBCTcor. The same phases as in figure 1 are shown.

		heart mean				
phase	modality	dose	left lung mean	left lung mean		
		(Gy)	dose (Gy)	ITV D ₉₈ (Gy)	(Gy)	
	СТ	1.3	16.7	58.9	50.2	
0	vCT	1.3	15.0	59.0	54.3	
	CBCT _{cor}	1.4	15.1	58.9	52.7	
	СТ	1.1	15.8	59.0	52.2	
3	vCT	1.2	14.6	58.9	52.1	
	CBCT _{cor}	1.3	14.8	58.9	53.4	
6	СТ	1.1	15.4	59.0	52.6	
	vCT	1.2	14.3	58.9	51.6	
	CBCT _{cor}	1.2	14.5	59.1	51.6	

<u>Abstract no 4:</u> Time-resolved estimated synthetic CTs based on orthogonal cine MRI for MR-guided proton therapy

Authors

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- ⁵ German Cancer Consortium (DKTK), Partner Site Munich, Munich, Germany
- ⁶ Department of Radiation Oncology, University Hospital Cologne, Cologne, Germany

Background

A method to create continuous time-resolved estimated synthetic CTs (tresCTs) based on orthogonal cine-MRI for potential use in MR-guided gated proton therapy of lung tumors was developed and its dosimetric accuracy was quantified.

Methods

A porcine lung phantom that reproducibly simulates respiratory-induced tumor motion was first imaged at a CT scanner, where a 3D-CT in mid-exhale breath-hold and a ground-truth (GT) 4D-CT during phantom motion were acquired. After transport to a nearby 0.35T MR-Linac, a 3D-MRI in mid-exhale breath-hold and interleaved orthogonal (sagittal/coronal) cine-MRI slices intersecting artificial gelatin tumors at 7.3Hz during phantom motion were acquired. The 3D-CT, 3D-MRI and orthogonal cine-MRI were input to a propagation method [1], which output 82s long tresCTs at 3.65Hz. Ten tresCTs were created for ten nodules in two porcine lungs. For each nodule, a robust IMPT plan (30×2Gy; 3 fields; 3% range robustness) was created on the GT-4D-CT mid-exhale image. An ITV to account for residual motion within a gating window was generated (3mm isotropic expansion of GTV). Each plan was recalculated on all GT-4D-CT phases and one randomly sampled tresCT per breathing phase. DVH parameter comparisons and gamma analyses were conducted for each nodule and breathing phase (100 dose comparisons).

Results

The median nodule motion amplitudes were 8mm (range 3-16mm). The tresCT and GT-4D-CT images and respective dose distributions showed high agreement (figure). The median relative deviations of the $D_{98\%}$, $D_{50\%}$, and $D_{2\%}$ were smaller than 1.1% for the ITV and GTV (table). The median gamma pass rate (global 2%/2mm criterion; 10% dose threshold) was 91.6%. Unaccounted lung density variations led to slight phase-dependent inaccuracies.

Conclusion

The proposed method could be applied for retrospective or real-time time-resolved accumulation of the delivered dose during MR-guided proton treatments in the future.

References

[1] Paganelli et al. (2018) JMIRO 62

Acknowledgements

DFG GRK2274

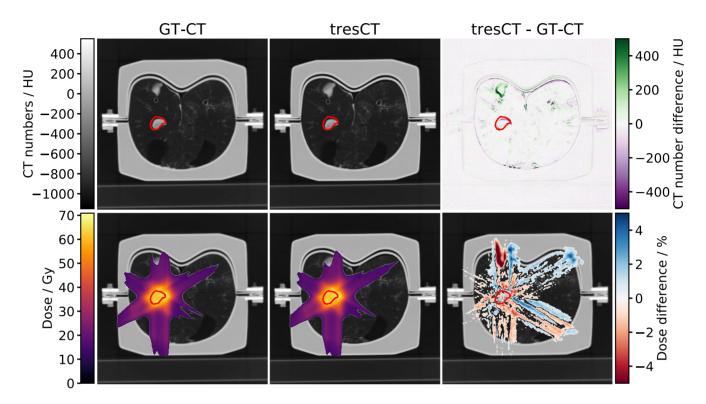


Figure: the figure shows exemplary ground-truth (GT; left column) and tresCT (center column) images, the corresponding dose distributions, and their differences (right column). The inhale phase is depicted, and the ITV is indicated as red contour.

Table: summary of the DVH parameter comparison analysis. The median [5th percentile, 95th percentile] relative deviations between the DVH parameters, defined as $(D_{tresCT}-D_{GT})/D_{GT}$, are given in percent for the ITV and GTV.

Structure	Parameter	Relative deviation / %
	D _{98%}	-0.9 [-2.4, 0.7]
ITV	$D_{50\%}$	-0.5 [-1.4, 0.2]
	D _{2%}	-1.1 [-3.2, 1.0]
	D _{98%}	-0.4 [-1.4, 0.8]
GTV	$D_{50\%}$	-0.3 [-1.0, 0.7]
	D _{2%}	-0.6 [-2.8, 1.8]

Abstract no 5: Lung cancer treatment experiences and planning strategies with pencil beam scanning carbon-ion beams

Authors

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Affiliations

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Background

Carbon-ion radiotherapy (CIRT) with the pencil beam scanning (PBS) technique for lung cancer has been carried out since 2015 in Shanghai Proton and Heavy Ion Center (SPHIC). In this report, we explain our experience of CIRT for lung cancer and present the techniques to deal with the interplay effect.

Methods

Most patients were immobilized in the supine posture with arms up to avoid an impact on treatment with lateral beam angles. GTV was contoured on the averaged CT and also on CT images of each phase. GTV on different CT images was combined to iGTV on the averaged CT. CTV was expanded from the iGTV. The plan optimization was performed using Syngo® TPS which incorporates the local effect model-I for converting physical dose to RBE-weighted dose distributions. Evaluation of the planning strategies were perfomed by generating four set of plans for 10 patients: The SBO-AsM (Single beam optimization with iGTV assigned to muscle) plans, the IMCT-AsM (intensity modulated carbon ion therapy with iGTV assigned to muscle) plans, the SBO-NoAs (SBO without tissue assignment) plans and the IMCT-NoAs (IMCT without tissue assignment) plans. PTV coverage and OAR doses of the plans recalculated on review 4D CTs (about 2 weeks and 4 weeks after the first treatment) were evaluated.

Results

The presented data shows the SBO-AsM plans provide better balance on the OAR dose than the others with the most optimal target coverage. The mean (minmum ~ maximum) V95% of PTV were 99.2% (98.0%-100.0%) and 98.0%(94%~99.9%) for the SBO-AsM plans recalculated on the review 4D CTs. A larger OAR dose variations could be observed for the IMCT strategies than the SBO strategies.

Conclusion

SBO-AsM strategy provides better target dose coverage. And, both strategies with IGTV assignment may result dose overshoot to deeper penetration depths.

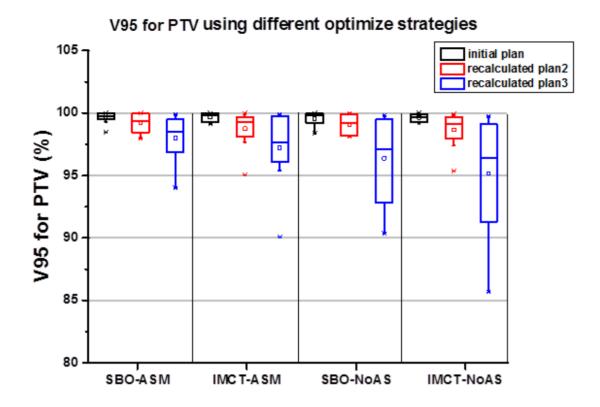


Figure 1: V95 for PTV use different planning strategies of the initial CT and reviewing CT display as box for 10 patients. The recalculated plan 2 and recalculated plan 3 were plan recalculated on the reviewing CTs. SBO-ASM and IMCT-ASM represent of SBO and IMCT strategies with iGTV assigned to muscle. SBO-NoAS and IMCT-NoAS represent of the SBO and IMCT strategies without iGTV assignment

<u>Abstract no 6:</u> Evaluation of interplay effects in pencil beam scanning proton therapy integrating the 4D XCAT phantom, the RayStation treatment planning system, and the AlignRT surface guidance

Authors

Christian Bäumer, Aaron Bley, Erik den Boer, Jörg Wulff, Ulf Mäder, Erik Engwall, Zoltan Perko, Beate Timmermann

Background

The dynamics of pencil beam scanning (PBS) applied to moving targets are known to induce a distortion of the dose distribution, which is called the interplay effect. The limited availability and artefacts of fourdimensional computed tomography images (4DCT) hamper the corresponding in-silico evaluation. This motivates the use of software phantoms for anatomical information, e.g., the 4D-XCAT phantom, and surrogate signals for the motion amplitude.

Methods

An XCAT phantom with 50 phases was combined with the RayStation treatment planning system (7.99.10). Deformable registration was used with time-resolved dose calculation, mapping XCAT phases to motion signals. Liver tumor cases with regular sin⁴-type motions were evaluated as clinical examples. Furthermore, variable breathing traces were integrated by a generic correlation between the amplitude of the AlignRT 3D camera system (Vision RT), which was evaluated at the sternum, and the amplitude of the diaphragm, which was extracted from 4DCTs of patients treated at the Westgerman proton therapy centre.

Results

The software framework enables researching the impact of the interplay and its mitigation. It allows for flexibility in determining motion management techniques and comparing alternative approaches. A case study with regular motion showed that the interplay effect was correlated with amplitude and strongly affected by the starting phase, leading to large local dose variances.

Conclusion

The integrated in-silico approach allows for a detailed analysis of motion in the context of PBS with comparable results to clinical cases. Flexibility in defining motion patterns for detailed anatomies in combination with a time-resolved dose calculation, facilitates the development of optimal 4D treatment strategies.

<u>Abstract no 7:</u> Exploring the potential of respiratory motion mitigation for lung cancer treatment with pencil beam scanning proton therapy using MRI – why enhanced DIBH is physically superior to highfrequency percussive ventilation

Authors

Emert F¹, Missimer J¹, Lomax A^{1, 2}, Weber DC^{1, 3, 4}

Affiliations

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Introduction

Precise irradiation of lung tumors using PBS proton therapy requires minimizing their mobility to ensure exact positional reproducibility and constant lung volume throughout the treatment. Therefore, two apnea methods for suppressing respiratory motion, enhanced-deep-inspiration-breath-hold (eDIBH) and high-frequency-percussive-ventilation (HFPV) were investigated with MRI in a clinical trial (NCT03669341) to establish inter- and intrafractional spatial variability.

Materials and Methods

During four sessions at weekly intervals, twenty-one healthy volunteers submitted to two 1.5T-MRIscans using both eDIBH and HFPV. To quantify positional changes, a lung-distance-metric was computed for 10 reference points distributed equally across the lung: a motion-invariant spinal cord and nine lungstructure-contours (LSCs: apex, carina, diaphragm, and six vessels) serving as tumor surrogates (Figure1). Measures of individual LSC spatial variabilities were introduced and lung volumes calculated by automated MRI-segmentation.

Results

While measures of lung volume remained constant, two vessels in the lower lung segment and the diaphragm yielded a two- to threefold improved positional stability with eDIBH, whereby absolute distance variability was significantly smaller for five LSCs (Table1). ≥70% of subjects showed significantly better intrafractional lung motion mitigation with eDIBH than with HFPV. Smaller ranges were most apparent in the anterior-posterior and cranial-caudal directions. All MRI-scans for each subject with eDIBH revealed maximum radial vessel displacements of 6.4mm (lower), 3.4mm (middle), and 2.9mm (upper) in the lung regions for 95% of the subjects.

Conclusions

Our data suggest that eDIBH outperforms HFPV regarding positional stability. An independent analysis demonstrated that physiologically optimized breath-holding (hyperventilation, 100%-O₂-supply, training) with full inspiration resulted in breath-suppression times in healthy volunteers that indicate pulmonary patients would be capable of breath-holding long enough to treat one irradiation field within a single eDIBH at Gantry2@CPT/PSI. Therefore, eDIBH provides easy-to-handle, effective, and efficient suppression of respiratory motion during proton therapy. It appears realistic to apply simplified 4D-treatment strategies under 3D-like conditions.

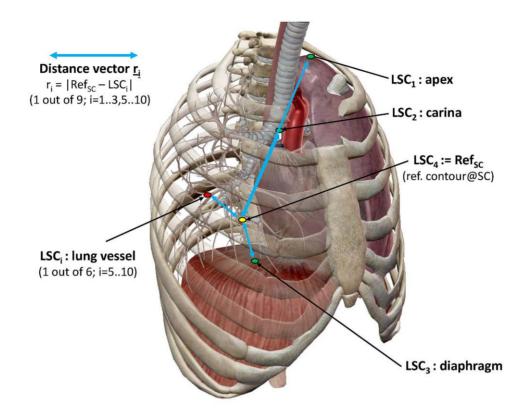


Figure 1: Representation of lung-structure-metric with selected LSCs. LSC distribution as described in the text (image courtesy of Visible Body[®]).

LSC	eDIBH	I	HFPV	р
	Media	Maximu	Media Maximu	m
	n	m	n	
	[%]	[%]	[%] [%]	
Apex	0.7980	1.3164	0.78763.2929	0.167
Carina	2.4417	3.8687	3.31487.1217	0.014
Diaphra	2.6896	9.3390	7.767125.0294	0.001
gm				
Vessel	1.1106	2.0416	1.24443.8462	0.218
Vessel	A 1.5520	3.0509	2.31863.5505	0.025
Vessel	1.7521	7.5847	3.794313.1986	0.010
Vessel _{RI}	1.4460 ر	1.9090	1.44874.3269	0.314
Vessel	м2.2613	7.0645	2.39316.3809	0.247
Vessel _{RI}	3.6881	16.3864	7.756621.1520	0.014

Relative errors of radial distances to reference/significance of difference

Table 1 : Median and maximum relative error [%] of radial distances between reference (Ref_{sc}) andselected anatomical structures (LSC_i), including significance of difference between correspondingdistributions of eDIBH and HFPV according to Wilcoxon signed rank test. Indexation of lung vessels:[L|R][L|M|U]=[Left|Right][Low|Mid|Up]

<u>Abstract no 8:</u> Impact of respiratory motion for breast cancer proton therapy in free breathing – evaluation of the first patients treated at the Danish Centre for Particle Therapy (DCPT)

Authors

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Background

Proton therapy for breast cancer is mostly treated in free breathing as breathing motion is assumed to have minor impact on the radiological path length when using an *en-face* field arrangement. This study examines the effect of respiratory motion in patients with breast cancer receiving loco-regional proton therapy based on 4DCT scans.

Methods

Twenty-five patients with breast cancer (20 left-sided, five right-sided) treated at DCPT in 2019-2020 were included. A planning CT in free breathing and a 4DCT (sorted in ten phases according to amplitude) were acquired for all patients. Breast or chest wall, internal mammary nodes (IMN), interpectoral nodes and level 1-4 lymph nodes were contoured as CTVs on the planning CT in free breathing. Patients were prescribed either 40 Gy RBE in 15 fractions (nine patients) or 50 Gy RBE in 25 fractions (16 patients). Clinical planning objectives: CTV breast/chest wall V95% and CTV lymph nodes V90% should be at least 98%. Proton therapy plans using 2-3 *en-face* fields, single-field optimisation and range shifter were created in Varian Eclipse v13.7. CTVs were robustly optimised using 14 worst-case scenarios: ±3.5% and ±5mm combined with ±3.5%. The proton therapy plan was recalculated on all ten phases of the 4DCT with fixed monitor units. All ten phases in the 4DCT were deformable image registered to the planning CT in Varian Velocity v4.0. Deformed doses from the phases were accumulated on the planning CT.

Results

The median (range) amplitude of respiratory motion measured at sternum position on the 4DCT was 2mm (1mm-4mm). Dosimetric results for the nominal plan and the 4D evaluation can be seen in Table 1. CTV coverage was below 98% for level 4 in one nominal plan and three 4D evaluations, for IMN in one 4D evaluation and for breast/chest wall in one nominal plan.

Conclusion

Respiratory motion has a low impact on the dose distribution in breast cancer proton therapy plans when using *en-face* beam arrangement and single-field optimisation.

	Nominal plan	4D evaluation	Absolute	
	(median, range)	(median, range)	difference	
			(median, range)	
Mean dose to heart	1.5 Gy RBE (0.5 to 3.4)	1.4 Gy RBE (0.5 to 3.5)	0.1 (-0.3 to 0.8)	
Mean dose to ipsilateral	8.8 Gy RBE (5.0 to 12.7)	8.2 Gy RBE (4.7 to 11.9)	0.3 (-1.0 to 0.8)	
lung				
CTV breast/chest wall V95%	99.7% (96.4 to 100)	99.6% (98.1 to 100)	0.0 (-2.5 to 1.4)	
CTV IMN V90%	100 (98.9 to 100)	99.6 (97.8 to 100)	0.2 (-0.3 to 2.2)	
CTV interpectoralis V90%	100 (99.5 to 100)	100 (99.5 to 100)	0.0 (-0.2 to 0.5)	
CTV level 1 V90%	100 (99.2 to 100)	100 (98.8 to 100)	0.0 (-0.7 to 1.2)	
CTV level 2 V90%	100 (99.4 to 100)	100 (98.9 to 100)	0.0 (-0.1 to 0.5)	
CTV level 3 V90%	100 (99.7 to 100)	100 (99.0 to 100)	0.0 (-0.3 to 0.7)	
CTV level 4 V90%	100 (97.9 to 100)	99.9 (96.3 to 100)	0.1 (-0.1 to 3.4)	

Table 1: Dosimetric results for the nominal plan, the 4D evaluation and the absolute difference (defined as the nominal plan minus the 4D evaluation).

<u>Abstract no 9:</u> Intensity-modulated proton therapy treatment delivery of locally advanced non-small-cell lung cancers within a single breathhold

Authors

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Objective

We studied the feasibility of pencil beam scanning (PBS) proton therapy treatments within a single breath-hold at PSI's Gantry 2. Treatment delivery time in PBS proton therapy depends on beam-on time and the dead time between proton spots (time required to change energy and/or lateral position). We studied ways to reduce beam-on and lateral scanning time, without sacrificing dosimetric plan quality, aiming at a single field delivery time of 15 seconds at maximum. We tested this approach on three lung cases with varying target volume.

Methods

To reduce the beam-on time, we increased the beam current at the isocenter by developing new beam optics for PSI's PROSCAN beamline and Gantry 2. Experimentally we obtained up to factor 5 higher transmission efficiency for all proton energies ^{1,2}.

To reduce the dead time between the spots, we used spot-reduced plan optimization³. First, a 3-field IMPT treatment plan was generated for all three-lung cases using the in-house clinical planning system 'PSIplan'. Spot-reduced plans were subsequently generated while mimicking relevant dosimetric plan parameters of the clinical plans to ensure comparable plan quality. The spot reduction technique reduced the number of spots by 94% compared with the clinical planning system for the lung cases considered (Table 1).

For the clinical and spot-reduced plans, 2-Gy(RBE) fractions were delivered with PSI's Gantry 2 using the clinical and transmission-efficient beam-optics, respectively. We extracted delivery times, including both beam-on time and dead time, from the log-files.

Table 1: Comparison of target sizes for the three lung cases, and the number of energy layers and spots per field for the different planning techniques.

	GTV(cm ³)	CTV(cm ³)	PTV(cm ³)	Treatment planning system	Field	Number of energy layers	Number of spots
Lung	727	998	1351	PSI plan	F1	50	14957
case					F2	68	11667
#1					F3	65	11529
				Spot	F1	46	1114
				reduction	F2	68	975
				plan	F3	54	482
Lung	342	538	754	PSI plan	F1	54	16275
case					F2	59	12251
#2					F3	59	12103
				Spot	F1	44	501
				reduction	F2	45	370
				plan	F3	55	490
Lung	107	216	369	PSI plan	F1	58	7857
case					F2	53	7860
#3					F3	40	7710
				Spot	F1	46	806
				reduction	F2	46	443
				plan	F3	34	537

Results

As shown in figure 1, a single field delivery with PSI plan and clinical beam optics takes about 40 to 100 seconds depending on the size, shape, and location of the target. The use of new optics and spot-reduced planning reduced delivery time by a factor of 4 to 6 and it is possible to deliver a single field within 15 seconds of the single breath-hold window for a very large lung case (lung case #1). For intermediate and small lung tumors (lung case #2-3), it is possible to deliver a field even within 7-10 seconds.

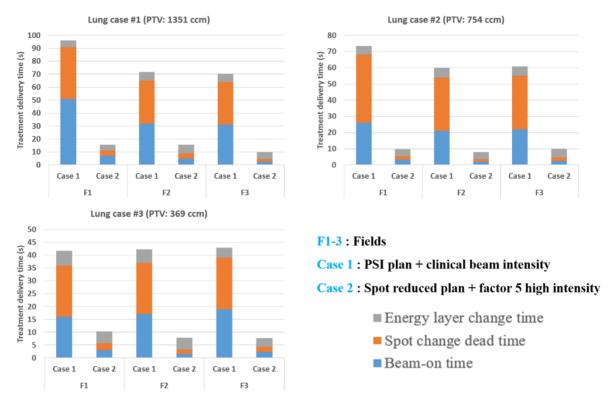


Figure 1 Treatment delivery time for different planning methods and beam line optimizations

Conclusion

In this feasibility study, we showed that it is possible to deliver a single field using intensity modulated proton therapy within a single breath-hold for locally advanced non-small cell lung cancers. To this goal, both beam-on time and dead time were shortened, using new beam optics in the delivery and spot reduction optimization in the planning. This is a very promising option to treat moving targets effectively with a breath-hold technique.

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Abstract no 10: Feasibility study for 4D CBCT at CNAO

Authors

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Background

The National Centre for Oncologic Hadrontherapy (CNAO) in Pavia is equipped with a custom robotic Carm mounted CBCT scanner (Fig.1a) [Fattori et al. 2015]. Such a system is currently used for setup correction and inter-fractional variations assessment in particle therapy. Previous studies highlighted the need for a daily depiction of the End-Exhale phase during gated treatments with particle therapy [Meschini et al. 2017]. The present study aims at assessing the feasibility of in-room 4DCBCT using such a custom system.

Methods

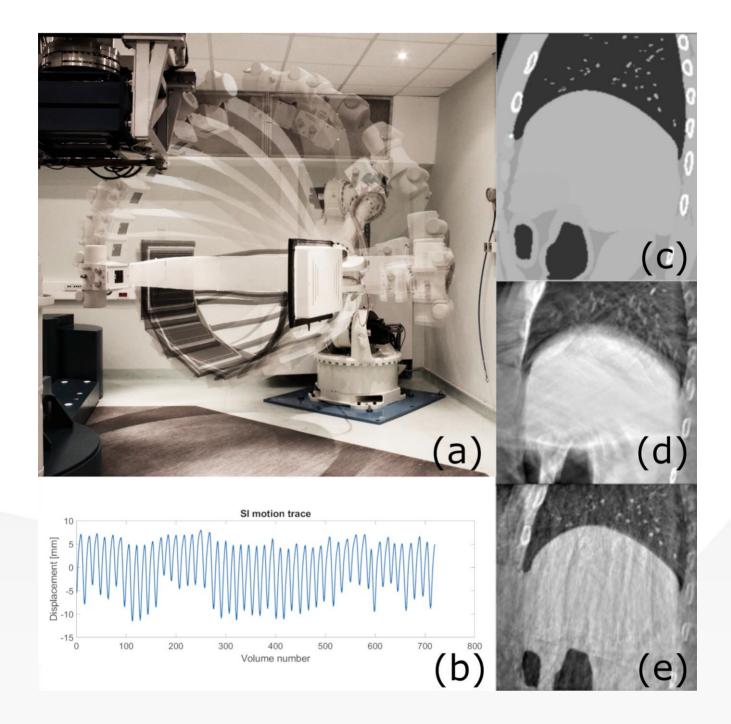
We forward projected the 4D extended cardiac-torso (XCAT) (Fig.1c) [Segars et al. 2010] phantom into the CNAO scanner geometry, generating virtual CBCT acquisitions with a known breathing surrogate. The acquisition trajectory is the same as a regular 3D CBCT (220°, 40s). Instead of a slower gantry we proposed a repeated acquisition protocol (220° x N). Regular and irregular breathing patterns (Fig.1b) (0% and 55.8% breathing irregularities with ranges of motion of 8 and 19 mm, respectively) were tested. For evaluation purposes, we studied (i) the effect of repeated acquisition in terms of CNR and (ii) the influence of the binning window width on Motion Blur (MB) at End-Exhale.

Results

The repeated acquisition protocol improves with maximum steepness around N=3 acquisitions (CNR=0.48). Regular/Irregular breathing patterns show MB of 0/0mm, 2/1mm and 2/2mm blur recovered at End-Exhale for three different binning windows of 0.33s (Fig.1e), 1s and 1.67s, against a 4/8mm from an average 3D reconstruction (Fig.1d).

Conclusion

We evaluated the feasibility of Full Fan 4DCBCT in the treatment room at CNAO using its custom imaging system during gated treatments. Improvements at End-Exhale of the 4DCBCT were observed in terms of motion blurring with respect to an average 3D reconstruction. Future studies will consider tests on the in-room system, along with evaluating phases other than End-Exhale.



<u>Abstract no 11:</u> Experimental validation of conformal motion mitigation through multi-phase 4D optimization implemented in the dose delivery system of CNAO

Authors

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Particle therapy can deliver more conformal doses compared to photon therapy, but this advantage is challenged by organ motion and motion uncertainty. Robust, conformal motion compensation is necessary to achieve clinical advantages over conventional therapy.

We propose a 4D-optimization strategy resulting in one treatment plan per motion phase, with a uniform dose to the PTV (or CTV combined with robustness scenarios) in each phase. These multi-phase 4D plans (MP4D) require a motion-synchronized delivery, which we implemented into the clinically used dose delivery system (DDS) of CNAO. For each beam energy, all plans are delivered with rapid switching between plans on detection of a motion phase plan.

The strategy has the following advantages: a) The plans incorporate a priori known range changes, b) the uniform dose in each phase provides inherent phase-controlled rescanning, and c) the plans to be delivered are known prior to delivery, enabling QA as opposed to other conformal strategies such as beam tracking.

The system was tested both at GSI and CNAO in experiments, including geometric plans to a motion including range changes, and patient plans in a QA-like setting, with doses reconstructed to water for comparison to measurements and to the patient 4DCT for DVH evaluation. Range changes could be compensated, and Gamma analysis (3mm/3%) showed >90% and >95% pass rate at GSI and CNAO, respectively. MP4D plans were significantly more conformal than range-ITV deliveries. We also analyzed the impact of irregular motion and delayed motion signals on the delivery.

The results for the delivery strategy are highly promising to result in a conformal motion mitigation strategy that is clinically more viable than beam tracking. We will continue to investigate MP4D in simulation studies and more complex experiments prior to a possible inclusion of MP4D in the clinically certified version of the DDS and subsequent clinical studies.

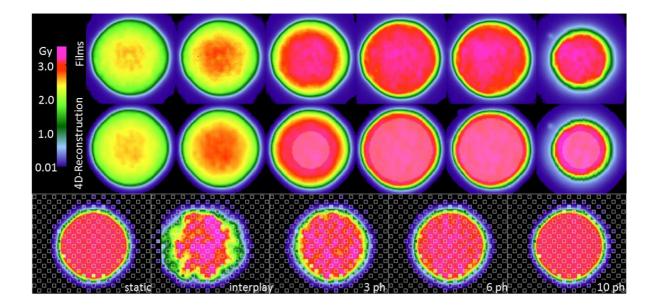


Figure 1: Results of film (top rows) and IC matrix detector measurements at GSI. The top row shows an MP4D delivery to a film stack behind a range-modifying phantom, with the corresponding 4D dose reconstruction below. The ellipsoid target is shaded in the dose reconstruction. The bottom row shows static, interplay and MP4D deliveries with 3, 6, and 10 phases with measurement (squares) plotted over a dose reconstruction. Motion was a 20 mm Lujan perpendicular to the beam.

Abstract no 12: Individualized daily setup robustness settings for head & neck IMPT using a library-of-plans

Authors

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Background

In intensity modulated proton therapy (IMPT), the impact of geometrical errors such as anatomical changes and varying patient position is typically minimized by using fixed setup robustness (SR) settings for the treatment course and patient population. However, the actual geometrical error varies per patient and per day.

This study explores an online-adaptive strategy based on a library-of-plans with increasing SR settings for head-and-neck (H&N) cancer patients. We evaluated the impact of daily plan selection on normal tissue complication probability (NTCP) and target coverage.

Methods

For 15 H&N patients treated with IMPT, a pre-treatment plan library was generated with 5 treatment plans robustly optimized for increasing SR settings: 0, 1, 2, 3, 5 mm, including 3% range error for all. For each repeat CT, a plan was selected based on target coverage. For evaluation, target coverage was accumulated probabilistically in 25 simulated treatment courses per patient. NTCP and the number of simulated treatments that complied with clinical target constraints in the library-of-plans strategy were compared to treatments with fixed SR of 3 and 5 mm.

Results

The library-of-plans resulted in a mean \geq grade-II xerostomia NTCP reduction of 3.8 ± 2.2%-point and a mean dysphagia NTCP reduction of 3.7 ± 2.5%-point compared to a 5 mm SR setting (Fig. 1, top). For 6/15 patients, the risk of a \geq grade II NTCP could be reduced by > 2%-point compared to 3 mm SR (Fig. 1, bottom). For four patients without NTCP improvement, target coverage pass rates were improved instead. In the library-of-plans strategy, 91.2% of the simulated treatments complied with all target constraints, compared to 82.1% and 94.7% in the 3 and 5 mm SR treatments (Table 1).

Conclusion

Significant NTCP reductions can be achieved by implementing a straightforward plan-of-the-day strategy. Furthermore, this strategy improved target coverage for selected patients reducing ad hoc replanning.

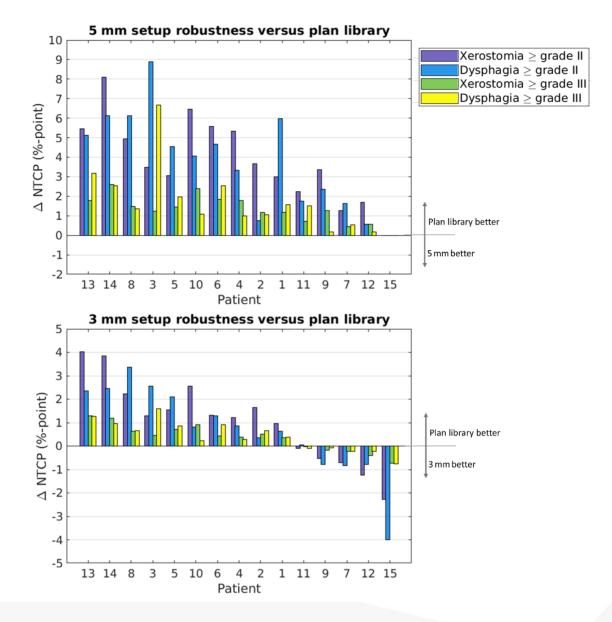


Fig. 1: Normal tissue complication probability (NTCP) differences for the plan library plans compared to 5 mm (top) and 3 mm (bottom) setup robustness settings for the risk of xerostomia and dysphagia ≥ grade II and ≥ grade III. Positive values indicate an improvement in the plan library strategy.
Table 1: Dosimetric pass rates accumulated target dose in 375 simulated treatments. Target coverage was accumulated probabilistically using 25 simulated treatment courses per patient with varying setup and range errors.

	CTV ₇₀₀₀ D _{98%} > 95% prescribed dose	CTV ₅₄₂₅ D _{98%} > 95% prescribed dose	CTV ₇₀₀₀ D _{2%} < 107% prescribed dose	Complies with all target constraints
0 mm	22.1%	16.8%	52.3%	4.0%
1 mm	53.9%	63.2%	85.9%	41.3%
2 mm	77.9%	89.9%	100%	69.6%
3 mm	89.1%	93.1%	100%	82.1%
5 mm	94.7%	100%	100%	94.7%
Plan Library	92.5%	98.9%	99.5%	91.7%

<u>Abstract no 13:</u> Treatment of mobile tumors in proton therapy synchronized with anatomy's motion

Authors

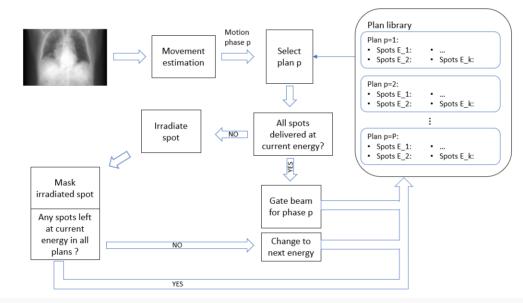
Valentin Hamaide¹, Kevin Souris², Damien Dasnoy¹

Purpose

The purpose of this work is to assess by simulation the treatment of moving tumors with scanned ion beams synchronized on the motion of a free-breathing patient.

Methods

A library of 3D plans is constructed where each plan corresponds to a conventional and independent treatment plan optimized on the CTV for each phase of a planning 4DCT. The anatomy's motion of a liver patient was recorded during several minutes using cine-MRI and transformed into a sequence of 3DCT's using the method of Dasnoy et al. [1] that follows the breathing pattern of a patient in 3D. The treatment is then delivered as follows: the closest planning 4DCT phase to the current 3DCT is selected based on the diaphragm position. The plan corresponding to that phase is delivered until the next image is obtained. The treatment coblz. 26 ook nientinues until all spots of the library of plans are delivered. If one or several phases would not be attained during the sequence (and thus the corresponding plans not delivered), the other plans compensate for the treatment plans not delivered by increasing the spot weight in the plan corresponding to the closest phase. A diagram of the treatment flow is outlined in the Figure below:



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Results

A treatment plan optimized on the Average CT with the ITV as target, a prescription of 60Gy and simulated on the free-breathing sequence of 3DCT's resulted in a D95 of 42.2Gy and a D5 of 59.6Gy on the CTV whereas our method resulted in a D95 of 56.6Gy and a D5 of 60.4Gy while also reducing the dose to the organs at risks.

Conclusion

Our strategy allows to deliver a more conformal dose to a mobile tumor compared to a conventional treatment plan while also reducing the dose to the organs at risks in a simulation case study.

References

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Abstract no 14: Effectiveness of motion mitigation techniques against breathing interplay effects in proton therapy

Authors

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Purpose

Breathing interplay effects arise from the interaction between the moving tumor and scanning beam. Several mitigation techniques and planning methodologies account for tumor motion during dose delivery, yet an in-depth comparison of how combinations of these perform is missing. This study aims to investigate the robustness of clinical plans when a wide range of mitigation approaches are applied during delivery.

Methods

We statistically evaluate interplay effects in 4D-CT and ITV plans (originally planned for 33 fractions of 2 Gy/fraction based on clinical practice at HollandPTC, Netherlands) of a lung cancer patient. The interplay dose calculation is based on a 4D-CT scan and a breathing signal indicating the phase at which each spot is delivered. We simulate several motion mitigation techniques, including fractionation, layered and volumetric rescanning, for a varying number of repaints and fractions, both with and without random extra time addition between spots or random energy layer ordering. Using 100 different breathing signals), our evaluation is based on the D₉₈ 90th percentile expressed as a fraction of the prescribed dose. Doses for hypofractionated treatments are adjusted to be biologically equivalent to the fully fractionated scenario.

Results

Our results show that the effects of adding more repaints in treatments delivered in more than 15 fractions are negligible, and that treatments delivered in 5 fraction with 5 repaints per fraction are almost equivalent to fully fractionated delivery. With similar values for the same number of repaints, we show that rescanning provides the same level of smoothing regardless of being volumetric, layered or including randomness. Finally, we demonstrate the inherent fragility of ITV plans compared to 4D-CT plans, as shown in the 4% decrease in D₉₈ across all settings.

Conclusions

We present a method to evaluate the effectiveness of motion mitigation techniques and apply it to show the robustness of 4D-CT plans and the added benefits of repainting in hypofractionated treatments.

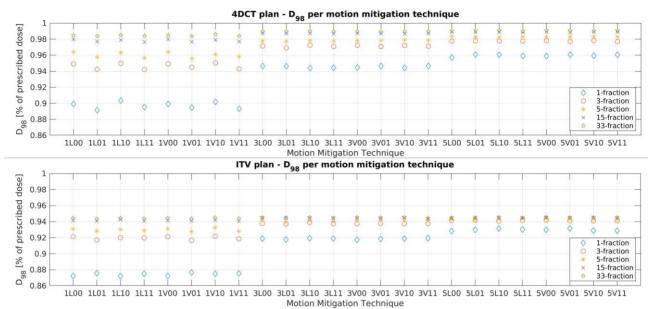


Figure 1: Dosimetric effect of motion mitigation techniques. For each mitigation approach, we report the 90th percentile of the distribution of D₉₈ values corresponding to 100 different interplay dose distributions. Each motion mitigation technique is identified with a 4 digit string, where each of the digits from left to right represent: number of repaints, type of repaint (L for layers and V for volumetric), randomness in the order of energy layers, randomness in the addition of extra time (where 1 denotes randomness). All results are reported for treatments delivered in 1, 3, 5, 15 and 33 fractions.

<u>Abstract no 15:</u> A physicist's perspective on the implementation and analysis of the first treatments of moving targets with protons at Maastro

Authors

Ilaria Rinaldi, Vicki Taasti, Esther Kneepkens, Gloria Vilches Freixas, Richard Canters, Wouter van Elmpt and Mirko Unipan On behalf of the proton thoracic teams at Maastro

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Background

Treatment of moving targets with particle therapy is considered a challenge. Various motion mitigation approaches have been investigated and clinically implemented in the last few years. At Maastro, we started treating patients with protons in February 2019 and our first lung cancer patient was irradiated in October 2019. In this contribution, we report on our clinical approaches to treat moving targets with the Mevion Hyperscan S250i.

Methods

We developed clinical workflows to robustly treat moving targets in the thorax region. We currently treat lung, lymphoma, and esophageal cancer patients. Patients are divided into two categories based on the tumor amplitude in the 4D CT: movements of less than 5 mm and between 5 and 20 mm, respectively. Amplitudes are defined based on the tumor excursions on the extreme breathing phases. For the first category, treatment planning is based on the CTV, while an ITV based strategy is used for the second category. A 3D robust optimization and evaluation are performed for both categories. An additional 4D robust evaluation is implemented for the tumors moving more than 5 mm to verify the dose in the different breathing phases. Furthermore, weekly repeated CT scans are acquired and evaluated.

Results

Until October 2021, we have treated 155 lung cancer (132 small and 23 large movers), 9 lymphoma, and 56 esophagus patients. Based on the weekly repeat CTs, we had to adapt the initial treatment plan for 23%, 50%, and 28% of the lung, lymphoma, and esophagus patients, respectively. We currently treat our patients in free-breathing, but we are investigating breathhold treatments as a complementary method.

Conclusion

We have developed and introduced a safe procedure to treat moving targets with protons at Maastro. The implemented clinical workflows are suitable for treating moving targets with a scanned proton beam within clinical tolerances. Our clinical approaches are continuously evaluated and improved.

Abstract no 16: CT reconstruction from single X-ray projection

Authors

Estelle Loÿen³, Damien Dasnoy-Sumell¹, Benoît Macq¹

Background

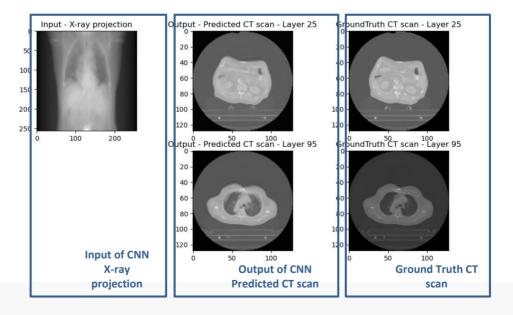
The treatment of abdominal or thorax tumor is challenging in particle therapy because the respiratory motion induces a movement of the tumor. One current option to follow the breathing motion is to regularly acquire one (or two) X-ray projection(s) during the treatment, which does not give the full 3D anatomy. The purpose of this work is then to reconstruct a 3DCT image based on a single X-ray projection to localize the tumor in 3D and in real-time.

Methods

To address this problem, we use a neural network that learns the mapping between a 2D X-ray projection and a 3D volume. This network, proposed by Henzler et al. in [1], consists of a deep CNN architecture composed of an encoder-decoder structure with skip connections. The learning dataset contains 500 3DCT images created by oversampling with random deformations of a planning 4DCT. Synthetic X-ray projections are then generated from the input CTs with the Tomopy library. This dataset is split on 90/10 basis for the training and test sets.

Results

The figure below illustrates one sample of the test set (Input of CNN) and two layers of the predicted CT scan (output of CNN) compared with the ground truth layers. To quantify the results, the normalized RMSE and the SSIM are computed and are equal to 0.04266 and 0.97495 respectively. To locate the mispredicted regions, a rigid registration is applied.



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Conclusion

This work allows the reconstruction of a CT image from a single X-ray projection, which will subsequently allow real-time tumor localization to improve treatment of mobile tumors.

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<u>Abstract no 17:</u> Assessment of dosimetric differences and sufficiency of margin approach, robust 3D optimization and best phase-plan scenario on creating clinically acceptable proton plans for various motion patterns

Authors

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Background

The robust optimization of a proton treatment plan is vital in order to account for uncertainties which may occur during the treatment delivery. The dosimetric sufficiency of an ITV approach, robust 3D optimization and best phase-plan scenarios where evaluated based on 4DCTs of a breathing phantom for various motion patterns.

Methods

CIRS Dynamic Thorax phantom with imaging rod insert of Ø3 cm, imitating lung cancer, was used for imaging and calculations. Three motion scenarios, monitored with the VisionRT system, were selected for the study (SI 5 mm, SI 10 mm and LAT 1.5 mm/AP 2.5 mm/SI 7 mm) and all 4DCTs were reconstructed to 10 breathing phases. Three different sets of treatment plans were calculated for each motion scenario: an ITV approach, robust 3D optimization and best phase-plans for subsequent breathing phases. In addition, the robustness analysis for the ITV and 3D optimized plans was validated against whole respiratory cycle to assess the possible dose deterioration effects.

Results

Dose metrics of 95% and 98% of the volume were selected for analysis. For all set of plans, both metrics presented clinically acceptable target coverage, overpassing 97% of the prescribed dose. Corresponding phase-plans were used as a benchmark to assess and evaluate the dosimetric differences for the ITV and robustly 3D optimized plans, which included 2 mm setup and 3.5% range error uncertainty. Thanks to the incorporation of different motion scenarios, the clinical significance and vulnerability of a specific approach was assessed.

Conclusion

The study presents dosimetric differences between an ITV margin approach, robust 3D optimization and best phase-plan scenario on a proton treatment plan quality. The results show that the single use of an ITV margin or robust 3D optimization may not be sufficient in specific cases to account for uncertainties occurring during the treatment delivery.

<u>Abstract no 18:</u> Identification of motion amplitudes in need for motion mitigation for synchrotron-based particle therapy

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Treating moving tumors at a synchrotron facility with a pulsed carbon ions poses challenges beyond the irradiation with a continuous proton beam. The decision on the treatment strategy for different indications requires the identification of motion amplitudes in need of motion mitigation.

Pencil beam scanned pulsed carbon and proton beams and the ARDOS breathing phantom [1] were employed: 8 motion scenarios, namely a tumor motion of 0.6, 1, 1.5 and 2cm alone and in combination with rib movement of 3mm and lung expansion of 2mm. SOBP treatment plans were created (RayStation 7.99) on the static CT to deliver a biologically-weighted dose of 2.0Gy for protons and 5.0Gy for carbon ions. The plans were delivered to the static and moving phantom synchronized with the beam. The dose was measured time-resolved (0.5s interval) using PinPoint (PP) ionization chambers (TM30013, PTW) inside (PP1-2, 5), in the penumbra (PP3) and outside the tumor (PP4). The layer specific dose rates were extracted from the dose delivery system log files. All measurements were performed starting from full-exhale position, while for the 2 cm tumor movement also the full-inhale starting point was investigated.

For the center of the tumor (PP2) the dose variation was 10% for all motion scenarios for carbon ions but only increased up to 5% for protons (Figure 1). PP5 exceeded the 10% deviation with the 2 cm motion scenarios for carbon, while the proton deviation was within 10% except for the full inhale phase. Dose deviations in the penumbra (PP3) increased by a factor of 2 for carbon ions compared to protons, ranging from 2 to 30% for increasing amplitude. PP4 in distal target region received in a static scenario less than 0.05Gy but increased up to 0.23Gy with motion. The dose rate influenced the results essentially.

The measurements confirmed the increased need for motion mitigation for carbon ions. The presence of rib and lung motion did not automatically deteriorate the results depending strongly on the chamber location. Although the target coverage was acceptable for most scenarios, regions adjacent to the tumor showed a pronounced dose deterioration.

References

[1] Kostiukhina et al (2019) Phys Med Biol 64:235001, doi: 10.1088/1361-6560/ab5132

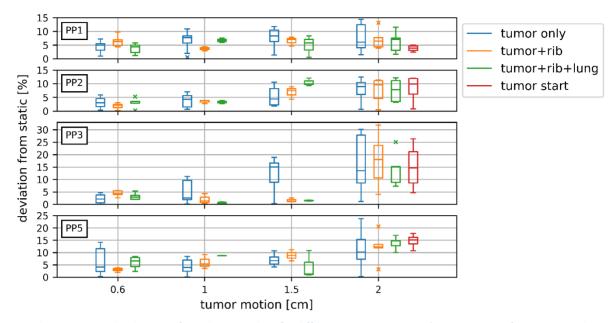


Figure 1 Boxplot containing the deviation from the static dose for different motion scenarios (tumor motion of 0.6, 1, 1.5 and 2 cm with and without rib and lung motions) for carbon irradiations. Each measurement was repeated at least 3 times. The red boxplot represents a different breathing starting phase.