Title

ATLAS-Based Active Bone Marrow–Sparing Intensity Modulated Radiation Therapy for Cervical Cancer

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prospective study. MRI may be important in objectively evaluating outcomes in breast cancer patients who undergo implant reconstruction.
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Prediction of Response to Radiation Therapy Treatment of Head and Neck Cancers Using an Artificial Neural Network Developed From Cone Beam Computed Tomography Image Textural Information

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Purpose/Objective(s): The aim of this pilot study was to investigate the feasibility of using CBCT textural information to construct an adaptive model for prediction of response to treatment for patients with head/neck (H/N) cancers.
Materials/Methods: Patients (N = 14) with H/N cancer were treated with radiation, 70 Gy in 35 fractions. Daily CBCT images were acquired for localization. Contours for targets and OARs were automatically segmented on each CBCT image set, by deformable registration of planning CT to CBCT datasets. Local control at 1-year was extracted, with 8 patients being classified as responders (R), and 6 as non-responders (NR). Textural features (22) describing patterns or spatial distribution of voxel intensities, extracted from gray level co-occurrence matrices were calculated from the tumor volumes. Two different artificial neural networks (ANNs) were constructed. The first ANN was based on those features able to provide statistically significant classification of the R and NR groups. For the second ANN, an independent method, Principle Component Analysis (PCA), was used to construct combinations of features that minimized the correlation between the features. Using the PCA components and Leave-One-Out Cross Validation (LOOCV) techniques, the ANNs were trained, optimized, and finally tested to predict outcome.
Results: Four textural features (Energy, Entropy, Homogeneity, and Maximum Probability) were found to be significantly different between the R and NR groups (see Table 1). However, these features were highly correlated. The first ANN, using these features as input, after training and optimization using LOOCV, was able to differentiate the R and NR groups with predictive power of 79%. PCA identified 4 parameters (consisting of weighted combinations of the 22 features), among which correlations were minimized. These parameters were then used as input into the second ANN, which differentiated the R and NR groups with predictive power of 78%.
Conclusion: This study demonstrates the feasibility of using textural features from CBCT images to predict outcome for H/N cancer patients. ANN's, developed using independent methods for feature selection, and produced similar results. The study is limited by the number of patients, which will impact the optimal features selected, and also render the models susceptible to Type II errors. Additionally, the textural features selected might be impacted by the intensities and contrast of the CBCT datasets. These factors, and the incorporation of additional outcome-related parameters into the model, are being investigated.

Abstract 221; Table 1. Data for the 4 features showing significant differences between responder and non-responder cohorts.

	Responders (N = 8)	Non Responders (N = 6)	Unpaired t-test
Selected Features	Mean ± SD	Mean ± SD	*P* Value
Energy	0.358 ± 0.085	0.556 ± 0.138	0.006
Entropy	3.304 ± 0.590	2.135 ± 0.816	0.009
Homogeneity	0.674 ± 0.053	0.796 ± 0.089	0.007
Maximum Probability	0.570 ± 0.077	0.730 ± 0.105	0.006

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Fully Automated Multicriteria Optimization (MCO) Treatment Plan Generation for Radiation Treatment Planning

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Purpose/Objective(s): To develop a novel multi-criteria optimization (MCO) solution approach to generate treatment plans without Pareto front navigation (any user-computer interaction).
Materials/Methods: Current MCO algorithms consider convex optimization problems and create an approximation of the Pareto front and then navigate over the approximation to obtain the final treatment plan. Our proposed method is able to handle nonconvex optimization optimization problems which includes dose-volume objectives/constraints, tumor control probability (TCP), normal tissue complication probability (NTCP), etc. In addition, instead of creating an approximation and navigation, our method targets the solution without any time-consuming human-computer interaction steps. This is achieved by a solution approach that utilizes given dose bounds on the structures by clinicians. We tested our method with 10 locally advanced head-and-neck cancer patients retrospectively using the concept of segment weight optimization. Monitor units were reoptimized using the segments extracted from the conventional intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT). We compared the results with conventional clinical plans and current MCO approach.
Results: Our MCO formulation had total 9 objective functions, which included 3 distinct objectives for primary target volume, high-risk and low-risk target volumes, 5 objectives for each of the organs-at-risk (OAR) (two parotid glands, spinal cord, brain stem, and oral cavity), and one for the non-target non-OAR normal tissue. Compared to the conventional clinical plan and current MCO method, the proposed MCO method achieved average reductions in left parotid mean dose of 8% ($P < 0.01$) and 7% ($P < 0.01$), right parotid mean dose of 12% ($P < 0.01$), and 8% ($P = 0.02$), oral cavity mean dose of 1% ($P = 0.63$) and 5% ($P = 0.28$) and spinal cord maximum dose of 28% ($P < 0.01$) and 10% ($P = 0.02$), brain stem maximum dose of 41% ($P < 0.01$) and 18% ($P = 0.01$), and normal tissue maximum dose of 9% ($P < 0.01$) and 8% ($P < 0.01$), respectively.
Conclusion: We proposed a novel MCO solution approach that generated superior high quality IMRT and VMAT treatment plans without any human-computer interactions.
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ATLAS-Based Active Bone Marrow–Sparing Intensity Modulated Radiation Therapy for Cervical Cancer

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Purpose/Objective(s): To test the hypothesis that atlas-based active bone marrow (ABM)-sparing intensity modulated radiation therapy (IMRT) can yield similar dosimetric results compared to custom ABM-sparing IMRT for cervical cancer patients.
Materials/Methods: Sixty-two cervical cancer patients treated at 4 institutions were randomly separated into training (N = 32) and test (N = 30) sets. All patients underwent pre-treatment FDG-PET/CT scans. Each PET/CT in the test set was registered to a common template using deformable registration, optimizing over the pelvic region. The set of deformed PET images was averaged to obtain the mean ABM distribution. The mean ABM

Abstract 223; Table 1. Mean DVH metrics (N = 15)

Structure	Metrics	PBM plan	ABM_{Custom} plan	ABM_{Atlas} plan	*P*
PBM	V_{10} (%)	83.0	82.2	82.1	0.83
	V_{20} (%)	61.6	59.6	57.5	<.001
	V_{30} (%)	41.2	38.2	36.7	<0.01
	V_{40} (%)	19.6	18.2	18.7	0.14
	D_{mean} (Gy)	25.6	24.9	24.6	0.02
ABM	V_{10} (%)	89.8	86.4	86.3	0.80
	V_{20} (%)	74.4	63.8	61.3	0.04
	V_{30} (%)	55.4	46.3	43.7	0.03
	V_{40} (%)	28.6	24.6	24.9	0.60
	D_{mean} (Gy)	30.0	27.3	26.8	0.08
Bowel	V_{30} (cc)	539.8	552.9	569.0	0.09
	V_{45} (cc)	154.9	156.1	158.6	0.46
	D_{max} (Gy)	49.1	49.5	50.2	0.01
Bladder	D_{max} (Gy)	48.2	48.4	48.5	0.37
Rectum	D_{max} (Gy)	47.6	47.8	48.1	0.10
PTV	V_{97} (%)	99.2	98.5	98.0	<0.01
	D_{97}(Gy)	45.0	44.8	44.6	<0.01
	V_{105} (%)	30.5	31.7	34.6	0.16
	V_{110} (%)	3.0	3.4	4.8	0.05

structure was then registered to each test patient using deformable registration, and ABM_{Atlas} was defined as the subvolume of the total pelvic bone marrow (PBM) with standardized uptake value (SUV) above the mean. For each test patient, a custom ABM (ABM_{Custom}) was also generated using the individual's actual PET/CT, by similarly segmenting the subvolume of PBM with SUV above the mean. Dice coefficients were used to measure the overlap of the two ABM subvolumes. Three different IMRT plans were generated for 15 randomly selected test patients, using the same objectives and priorities for all structures, except for an additional avoidance structure for PBM, ABM_{Atlas}, or ABM_{Custom}. All plans were normalized with PTV $V_{100\%}$ to 95%. Both DVH metrics and NTCP (PMID: 20400238), were used as plan quality indicators. Paired t-tests were used to test differences between ABM_{Atlas} and ABM_{Custom} plans.

Results: We observed no significant difference in ABM_{Atlas} vs. ABM_{Custom} absolute volumes. The mean Dice coefficient between ABM_{Atlas} vs. ABM_{Custom} was 0.74 (range: 0.64-0.86). Surprisingly, ABM_{Atlas} plans outperformed the other two plans in terms of PBM and ABM sparing (Table 1). The estimated mean white blood cell count (WBC) nadir (based on V_{20}) for ABM_{Custom} plans vs. ABM_{Atlas} plans was 3.11 vs. 3.25 ($P < 0.001$), indicating superiority of the atlas-based ABM sparing approach for reducing NTCP.

Conclusion: Atlas-based ABM sparing IMRT is feasible and may obviate the need for custom PET-based ABM-sparing approaches as a strategy to reduce hematologic toxicity.

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On-Board Molecular Imaging (OBMI) for Radiation Therapy

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Purpose/Objective(s): On-board imaging with cone-beam CT became the clinical standard in radiation therapy. Additional molecular information would allow physicians to precisely stage the response of previous cancer therapy online. The molecular information can be used to directly adapt dose or field geometries and can be incorporated in later treatment planning. The feasibility to realize x-ray fluorescence (XF) molecular imaging by an added detector device for existing OBI systems is studied.

Materials/Methods: XF computed tomography (XFCT) requires detectors with directional information when combined with cone-beam sources of OBI systems. In this regard, the feasibility of a Compton camera is examined on the basis of Monte-Carlo simulations for the fluorescence of gold nanoparticles. A sandwich camera composed of 3 mm Si and 1 mm CdTe is used, which is an optimization for energies of K-shell fluorescence. As excellent energy resolution is necessary to distinguish fluorescent photons from scatter background and to increase the directional precision, the resolutions were selected close to their physical limit of 140 eV and 800 eV, respectively. The imaging capabilities are examined in three setups for the clinical scenario of a lung scan. The detection system comprises four 16 x 26 cm^2 large detector panels which are placed on the chest of the phantom (back-scatter configuration). The first setup investigates the spatial resolution capability where 2 mm spheres with 10% gold solutions are placed on different detector distances. The second setup determines the detectability limits for different cone angles for lesions with gold concentrations ranging from 0.05% to 2%. Third, the impact of the x-ray source spectra is analyzed for a monochromatic x-ray source and a measured OBI spectra. Image reconstruction is performed with a list-mode MLEM algorithm with cone-projector on a GPU.

Results: In the spatial resolution setup, the FWHM of the reconstructed sources after 30 iterations decreased from 3.1-5.7 mm for lesions in a detector distance of 4-14 cm, respectively. The detectability limit for lesions worsens from 0.3% to 1.6% gold concentrations for increased cone angles from 0.2° to 5°. For the monochromatic x-ray source, the detectability is improved to 0.1% - 0.9% for the 0.2° and 5° cone angles.

Conclusion: The study shows that the combination of XFCT and Compton scatter imaging is a valid path to realize molecular imaging with high atomic number probes for radiation therapy. Existing OBI systems can be upgraded with the suggested detector technology to enable molecular imaging, but adapted radiation sources would further increase the molecular sensitivity. Given the constraints of energy resolution and limited exposure dose, spatial resolutions of some mm and molecular sensitivities in the nM range are accessible.

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A Biomechanical Modeling Guided Cone Beam Computed Tomography Reconstruction Technique

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Purpose/Objective(s): We developed a Bio-recon technique to improve CBCT reconstruction accuracy using limited-view projections. Bio-recon also solves inter-fractional patient deformation fields as a side product, which facilitates potential tumor tracking, dose accumulation, and adaptive radiotherapy.

Materials/Methods: We reconstructed the new CBCT image by deforming a prior high-quality CT/CBCT image using a deformation vector field (DVF). The DVF was iteratively optimized during reconstruction, so that the 2D projections generated from the reconstructed CBCT matched the clinically acquired projections. The deformation-based reconstruction was referred as "2D-3D deformation." Bio-recon combined 2D-3D deformation

Abstract 225; Table 1. (Mean ± Standard deviation) Reconstruction results of different techniques for all 11 patients.

	Relative errors of reconstructed CBCTs			DVF errors as compared to manually tracked anatomical landmark motion		
Number of projections	FDK	2D-3D deformation only	Bio-recon	FDK	2D-3D deformation only	Bio-recon
5	75.2 ± 9.0%	13.2 ± 2.3%	12.3 ± 1.8%	N.A.	5.5 ± 4.1 mm	3.5 ± 2.9 mm
10	58.5 ± 6.0%	12.0 ± 2.3%	10.4 ± 1.3%		5.6 ± 4.3 mm	3.1 ± 2.4 mm
20	48.7 ± 4.0%	9.4 ± 1.2%	8.9 ± 0.9%		4.8 ± 3.8 mm	2.9 ± 2.1 mm