Utilizing Knowledge-Based Planning Model to Predict Achievable Prescription dose for Mesothelioma Patients with Two Intact Lungs

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Introduction:

Malignant Pleural Mesothelioma (MPM) can be successfully treated with trimodality therapy consisting of surgical pleurectomy/decortication, chemotherapy and conventionally fractionated hemithoracic intensity modulated pleural radiation therapy (IMPRINT)[1], ideally to a prescription dose of 50.4 Gy. These are complex plans that typically use 8-10 beam directions for IMRT or 4-6 arcs for VMAT(Figure 1). We have previously demonstrated that the contralateral to ipsilateral lung volume ratio (CIVR) can help to predict the maximum attainable prescription dose for these treatments [2]. However, CIVR can only predict two categories (≥48.6 Gy or ≤46.8 Gy) of prescription dose and cannot predict prescription limitations due to doses to other critical organs such as heart or liver or key dosimetric indices for risk organs.

Therefore, we created two knowledge-based planning (KBP) models in a commercial treatment planning system for right- and left-sided MPM cases. These models can predict mean doses and other objectives to specified risk organs, thus can be use to predict achievable prescription and quickly suggest initial optimization objectives which leads to more consistent plan quality and significantly reduces time-consuming trial and error during planning.

Methods:

Delivered IMRT/VMAT plans (1.8 Gy/fraction, 23-28 fractions) for 55 right and 42 left-sided patients were used to create a KBP model for each side in Eclipse treatment planning system V15.5 (Varian Medical Systems, Palo Alto, CA). To validate these models, the differences between predicted and clinically planned mean organ doses (MODs) for lung (MLD), liver and heart were evaluated for an additional 7 right and 8 left-sided cases. We developed a formula to predict potential achievable mean lung dose (MLD) for an input prescription. The highest achievable prescription dose (HAPD) is the highest prescription at which $MLD_{prediction}$, given by Eq 1, is less than 20.5 Gy:

$$MLD_{prediction}=MLD_{model}+D_{mean\ diff}+D_{stdav\ diff} \qquad (1)$$

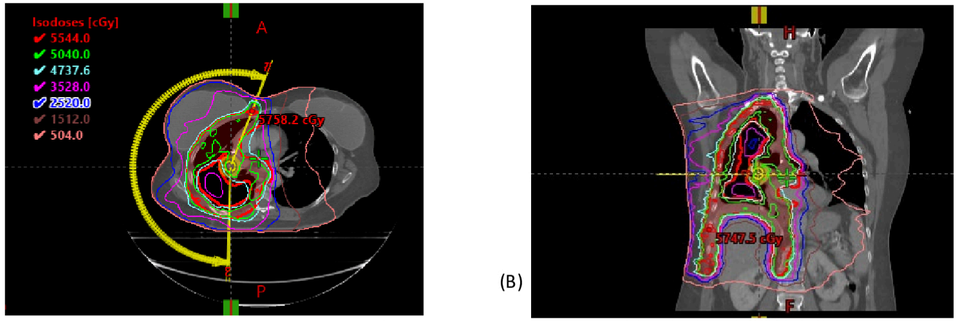
Where $MLD_{predivtion}$ is the predicted MLD; MLD_{model} is the MLD predicted by the KBP model; $D_{mean\ diff}$ and $D_{stdav\ diff}$ are the mean and standard deviation of difference between MLD_{model} and the MLD in the clinical plans for the validation patients. For new cases, the planning scan, contours and proposed prescription are the inputs. The MLD and other objectives predicted by the KBP provide initial multiple patient-specific optimization objectives for the new case. This approach was used to retrospectively re-plan 9 test cases (6 right, 3 left) for which the clinical plan disagreed with HAPD predicted by a different published method (6/9 cases) or where target coverage could be improved.

Results:

KBP reports objectives in approximately 5 to10 seconds. Figure 2 is the boxplots of mean dose difference between the KBP prediction and clinical validation plans. The mean and standard deviation of the difference of mean lungs, heart and liver dose between predicted and clinical plan for right and left sided models are (159.2±73.8; 113.8±185.5; 339.6±271.4 cGy) and (174.5±51.0; 256.4±118.1; 155.3±144.0 cGy), respectively. Table 1 is the result of re-optimizing 9 additional cases using the HAPD and the objectives generated from the KBP models as initial optimization parameters. 7/9 re-planned test cases met all our clinical planning constraints at predicted HAPD; two met lung but not other normal tissue constraints at HAPD. With MLD approximately 20 Gy, the median difference between predicted and re-planned MLD was -0.018 Gy (range -31 to 92 cGy).

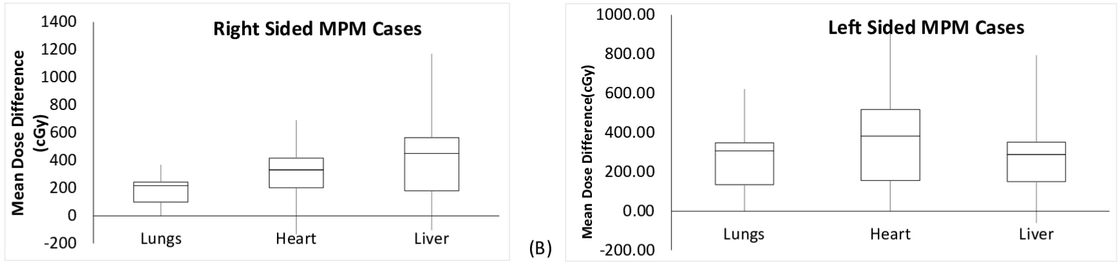
Conclusions:

KBP models built from previously treated cases efficiently predict the HAPD for hemithoracic IMRT plans to treat mesothelioma and provide starting optimization objectives for plans to achieve this prescription. This method may help different institutions to efficiently achieve consistent quality plans in the NRG LU006 protocol (NCT04158141), a randomized phase III trial to evaluate survival benefit of IMPRINT.



(A) (B)

Figure.1. Typical hemithoracic pleural IMRT plan for MPM. PTV is represented by thick red lines: (A)beam arrangements and isodose distribution on axial view, (B) isodose distribution on coronal view.



(A) (B)

Figure.2 The boxplots of mean dose difference between the KBP prediction and clinical validation plans for right sided MPM cases (A), and left sided MPM cases (B).

(cGy)				MLD at the HAPD		
Case	Clinical PD	CIVR PD	HAPD	$MLD_{prediction}$	New plan	Note
Case 1	4500	≤4680	5040	2018.7	2020.5	
Case 2	4500	≤4680	4500	1981.7	2005.4	
Case 3*	4860	≤4680	4680	1983.7	1933.1	Plan of HPAD=4860 can meet clinical constraints
Case 4	4500	≥4860	4860	1989.9	2020.0	Can't meet other clinical constrains
Case 5	4500	≥4860	4860	2009.4	2030.0	
Case 6*	4860	≤4680	4500	2020.7	2042.7	
Case 7	4680	≥4860	4680	2022.3	2004.9	
Case 8	4680	≥4860	5040	2035.3	1943.0	
Case 9*	5040	≤4680	4860	1998.9	1977.3	Can't meet other clinical constrains

Table.1 Clinical prescription dose (PD) verses CIVR PD and HAPD; MLD of HAPD in MLDprediction and new plan for 9 test cases

References:

1. Rimner A, Zauderer MG, Gomez DR, et al. Phase II Study of hemithoracic intensity-modulated pleural radiation therapy (IMPRINT) as part of lung-sparing multimodlity therapy in patients with malignantpleural mesothelioma. JCO 2016;34:2761-2768.
2. Kuo, L., Yorke, E.D., Dumane, A.V., et al. Geometric dose prediction model for hemithoracic intensity-modulated radiation therapy in mesothelioma patients with two intact lungs. J Appl Clin Med Phys. 2016;17: 371-379