Functionally Weighted Airway Sparing (FWAS) to preserve post-SAbR respiratory function

E. VICENTE [1], A. MODIRI [1], J. KIPRITIDIS [2,3], A. HAGAN [1], K. YU [4], H. WIBOWO [4], Y. YAN [5], D.R. OWEN [6], M.M. MATUSZAK [6], P. MOHINDRA [1], R. TIMMERMAN [3], A. SAWANT [1]

[1] University of Maryland School of Medicine, Baltimore, MD, USA
[2] Northern Sydney Cancer Centre, Sydney, Australia
[3] CRF Image X Institute, Sydney, NSW, Australia
[4] Broncus Medical, Inc., San Jose, CA, USA
[5] UT Southwestern Medical Center, Dallas, TX, USA
[6] University of Michigan, Ann Arbor, MI, USA

JULY 12–16 2020 VIRTUAL JOINT AAPM | COMP MEETING
EASTERN TIME [GMT-4]

INNOVATION/IMPACT

- The FWAS method [1] disrupts the existing idea in functional lung avoidance radiotherapy (FLAR) of focusing on the sparing of functional lung tissue regions alone.
- The innovative idea is that FWAS reduces radiation damage to the airways that serve high-functioning lung regions, overcoming the limitation of FLAR techniques where dose redistribution based solely on functional lung maps may cause irreparable damage to the "supply chain" of high-functioning lung sub-volumes.
- The initial results illustrate the potential to reduce the probability of post-SAbR loss of respiratory function.

METHODS

Patient data

As a proof of concept, we used data from lung SAbR patients from an IRB–retrospective cohort (Table 1). 3D conformal SAbR (CRT) was prescribed for all four patients and used as the reference to compare with the proposed method performance.

The functionally weighted airway sparing (FWAS) method

The method estimates the desire avoidance of dose in each airway tree element in the RT plan, considering their contribution to the ventilation observed in the functional map (Fig. 1). Steps:

Step 1 **Sub-lobar volumes definition**: Each terminal airway is connected with the closest lung voxel, defining as many sub-lobar volumes as segmented terminal airways. Defined on the Breath-hold (BH) CT image.

Steps 2 & 3 **4DCT-based ventilation map calculation**. Using the Hybrid metric and VESPIR [2,3]. The map (defined on the 4DCT-exhale phase) is registered (DIR) to the BHCT.

Step 4 **FWAS map estimation**. The ventilation in each sub-lobar volume is calculated using the ventilation map and then assigned to the airways connected to the sub-lobar volume (Fig. 2).

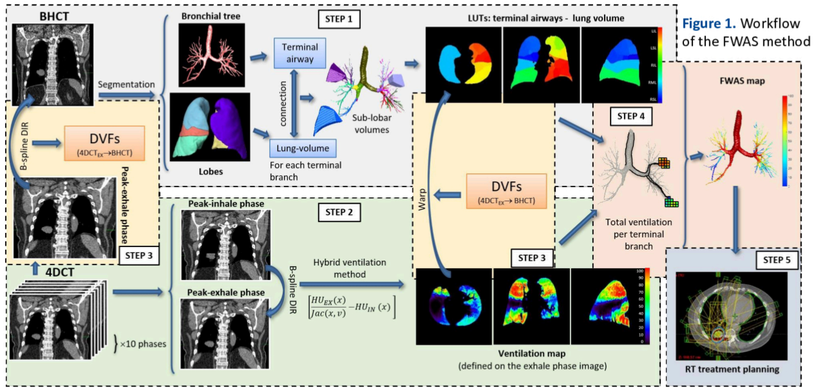

Figure 1. Workflow of the FWAS method

Patient	Tumor location	Information
P1		• 59-year-old woman • PTV: 112.53 cc (LUL, central, anterior) • Prescription: 10 Gy × 5 fractions (11-beam CRT) • Seg. airways: 251 • Seg. terminal airways: 127 • Seg. max generation: 12
P2	This patient has no LUL (surgically removed)	• 55-year-old woman • PTV: 11.98 cc (LLL, posterior) • Prescription: 12 Gy × 5 fractions (10-beam CRT) • Seg. airways: 166 • Seg. terminal airways: 84 • Seg. max generation: 12
P3		• 75-year-old man • PTV: 96.76 cc (between RUL and RML, posterior) • Prescription: 12 Gy × 5 fractions (13-beam CRT) • Seg. airways: 239 • Seg. terminal airways: 119 • Seg. max generation: 11
P4	RUL RLL	• 62-year-old man • PTV: 19.85 cc (RUL, centre) • PTV: 7.76 cc (RLL, posterior) • Prescription: 18 Gy × 3 fractions (10-beam CRT) for each PTV • Seg. airways: 203 • Seg. terminal airways: 102 • Seg. max generation: 12

Table 1. Patient demographics and treatment details for the proof of concept study.

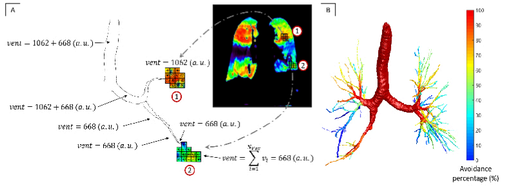

Figure 2. A: 2D example of FWAS map generation. The ventilation in vol 1 (1062 a.u.) is assigned to the terminal airway connected to this volume and to the rest of the upstream airways. Same process for ventilation in vol 2 (668 a.u.). Because some upstream airways also contributed to the ventilation of vol 1, both contributions are summed up in those airways. **B**: By repeating this process for all the sub-lobar volumes, we obtained the FWAS map (3D map for P3 in fig.).

Step 5 **FWAS plan**: PSO–based [4,5] treatment planning system including the airways as organs at risk (OARs).

Objective function: $F = \sum_{i \in OARs\ \&\ PTV} \left(D_i - D_i^c\right)^2 \times f_i + \sum_{i=1}^{N_{airways}} w_i \times \left(D_i - D_i^c\right)^2 \times f_i$

Airways term; Functional weights (FWAS map)

$f_i(lower) = \begin{cases} 1, & if\ D_i < D_i^c \\ 0, & if\ D_i \geq D_i^c \end{cases} \quad i \in PTV; \quad f_i(upper) = \begin{cases} 1, & if\ D_i > D_i^c \\ 0, & if\ D_i \leq D_i^c \end{cases} \quad i \in OARs, PTV\ \&\ Airways$

Max dose to keep the airway open

$D_i^c = D_{max}\ (Pr_{coll} = 0.05)$
$= D_{max}\ (Pr_{op} = 0.95)$
$= 9.8 + 3.7 \times d$

Airway radiosensitivity (prob. airway collapse)

$Pr_{coll} = \frac{1}{1 + e^{-(\alpha_1 + \alpha_2 \cdot d + \alpha_3 \cdot D_{max})}}$

Prob. airway open or no collapse
Airway diameter

RESULTS

Performance evaluation of the FWAS method

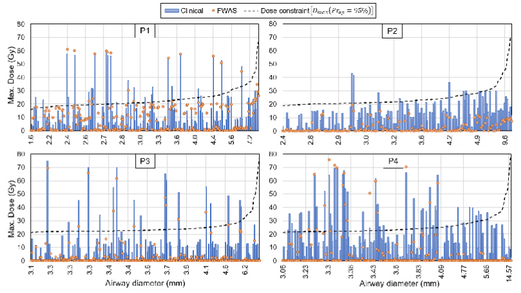

Figure 3. Maximum dose delivered to the airways in the Clinical (blue bars) and FWAS (orange circles) plans for the four patients (P1–P4). The dose constraints used in the FWAS plan are shown as black dashed lines.

The superior performance was also reflected in a higher ventilation due to airflow through open airway paths after treatment for the four cases (Fig. 5) compared to the prescribed clinical plans (Clinical) and the inverse-optimized clinical plans (PSO-Clinical).

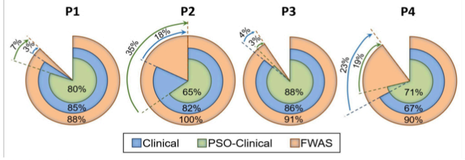

Figure 5. Ventilation preservation due to airflow through open airway paths (Pr_{op} = 95%) for the Clinical (blue sectors), PSO-Clinical (green sectors) and FWAS (orange sectors) plans for the four patients (P1–P4). The improvement achieved with respect to the Clinical plans are presented as blue arrows and as green arrows with respect to the PSO-Clinical plan.

The FWAS plans showed to reduce the dose with respect the clinical plan (Fig. 3) and, consequently, the probability of collapse in the overdosed airways (dose over the estimated dose constraint for collapse) located ≥5 mm from the PTV (Fig. 4), demonstrating superior performance in redistributing the dose with respect to the clinical plan. Clinical dose-volume constraints were met for both methods for OARs (esophagus, heart, spinal cord, and lungs) and PTV.

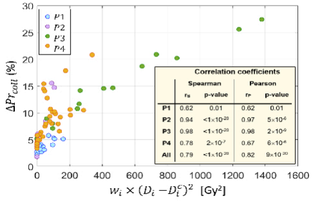

Figure 4. Statistical correlation (for airways located ≥5 mm from the PTV for the 4 patients [P1–P4]) between the reduction in probability of airway collapse ($\Delta Pr_{coll} = Pr_{coll}^{clin} - Pr_{coll}^{FWAS}$) and the airways term in the objective function in the FWAS method, $w_i \times \left(D_i - D_i^c\right)^2$. Highly significant ($p \leq 0.01$) values in Spearman coefficients (0.62–0.98) confirmed a monotonic behavior, and highly significant ($p \leq 0.01$) Pearson coefficients (0.62–0.98) confirmed a linear correlation.

Impact of DIR errors on the FWAS method

We conducted a sensitivity analysis to study the contribution of the ~2 mm average B-Spline DIR uncertainty of the software used [2] on the FWAS method by estimating the uncertainty in ventilation in the sub-lobar volumes connected to the terminal airways (Fig. 6).

Uncertainties were < 10% for 95% of the volumes and < 6% for 82%. Higher uncertainties were found for lower ventilation values. Errors were <10% for ventilation values >20%. Therefore, airways connected to higher ventilated volumes (the important ones in the FWAS method) were less affected by DIR errors.

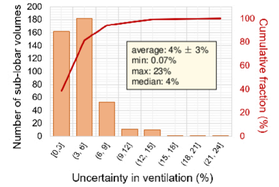

Figure 6. Distribution of the uncertainties in ventilation (orange bars) in the FWAS sub-lobar volumes due to B-spline DIR errors.

CONCLUSIONS

- This work shows that it is possible to include the airways as OARs in SAbR plans without compromising the clinical dose constraints of the commonly used OARs and ensuring coverage of the PTV.
- The proposed FWAS method shows that it is feasible to reduce the dose delivered in high-functional airway paths, resulting in a higher lung function after treatment.
- By reducing the probability of post-RT toxicity, such methods may lead to expansion of the use of SAbR to a wider population.
- Although this method may be cumbersome with currently available clinical tools, the basic framework can be largely automated for eventual clinical implementation.

ACKNOWLEDGEMENTS

- **Funding support:**
National Institutes of Health (R01 CA202761)
"Investigating Radiation-Induced Injury to Airways and Pulmonary Vasculature in Lung Stereotactic Ablative Body Radiotherapy (SAbR)".

REFERENCES

[1] Vicente E. et al. Phys. Med. Biol. 2020 (Accepted). [doi:10.1088/1361-6560/ab9f5d]
[2] Kipritidis J. et al. Med. Phys. 2014;41(1):011910. [doi:10.1118/1.4856055]
[3] Kipritidis J. et al. Med. Phys. 2015;42(3):1255-67. [doi:10.1118/1.4907991]
[4] Modiri A. et al. Phys. Med. Biol. 2016;61(16):6181. [doi:10.1088/0031-9155/61/16/6181]
[5] Aaron H, et al. Phys. Med. Biol. 2018;63(2):025028. [doi: 10.1088/1361-6560/aa9c96]

CONTACT INFORMATION

Esther Vicente: evicente@som.umaryland.edu