EVALUATION OF RADIOGRAPHIC PULMONARY CHANGES ON SERIAL CHEST CT SCANS AFTER RADIATION THERAPY FOR BREAST CANCER: A COMPARISON OF PROTON VS. PHOTON THERAPY

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I. INTRODUCTION

- There are now over 3.5 million long-term breast cancer (BC) survivors in the United States.[1]
- Radiotherapy (RT) is a critical component of breast cancer management, yielding a substantial survival benefit[2] but can result in inadvertent exposure of large volumes of normal tissues to low and moderate doses of radiation.
- 14% of Breast Cancer patients treated with radiation develop clinical pulmonary toxicity, with 4% overall experiencing high-grade clinical toxicity.[3]
- Compared to photon therapy, proton therapy often results in improved lung dosimetry but a clinical benefit in terms of decreased lung toxicity has not yet been quantified.

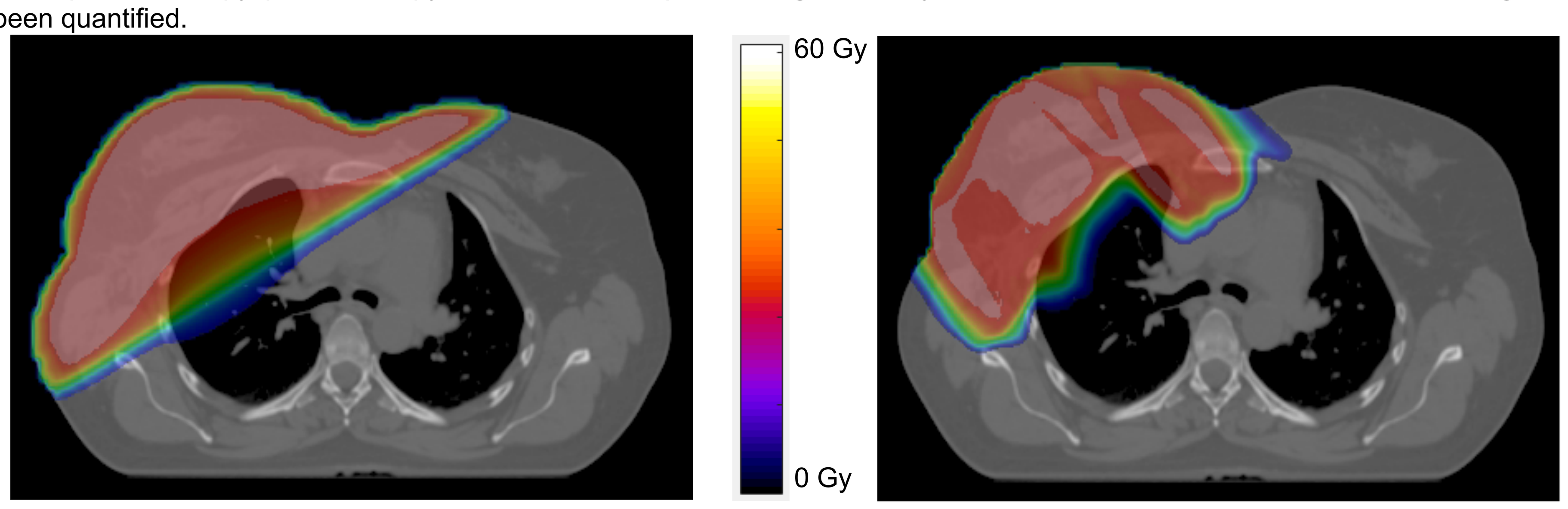

Figure 1: **Treatment Planning for Photon vs Proton Therapy**: These figures represent radiation treatment planning on chest CT scans for right sided breast cancer patients. The colors represent the distribution of radiation exposure. The figure on the left shows radiation treatment planning for conventional X-ray based photon therapy and the figure on the right shows a comparative plan for the same patient but for proton therapy treatment.

OBJECTIVE : Assay radiographic pulmonary changes on serial chest CTs after radiation therapy for breast cancer (Stage II or higher) undergoing conventional photon vs proton therapy.

II. METHODOLOGY

IMAGE ACQUISITION

- Images were acquired involving 64-slice CT systems with 1x1x1 mm voxel dimensions, typically using a non-ionic contrast agent and breath-holding for motion correction. Images were acquired at Pre-Treatment and 1, 3, 6, 12 and 24 months post RT
- To date, 25 patients have been enrolled in the study, with 88% (22 of 25) and 44% (11 of 25) attaining 6 month and 1-year follow-up, respectively.

IMAGE REGISTRATION AND LUNG MASK EXTRACTION

- The follow up CTs were registered to Planning CT where the dose was defined, using in-house software.
- The lung mask was extracted[4] from the follow-up CT under examination by subtracting all other structures from the original lung CT image set.

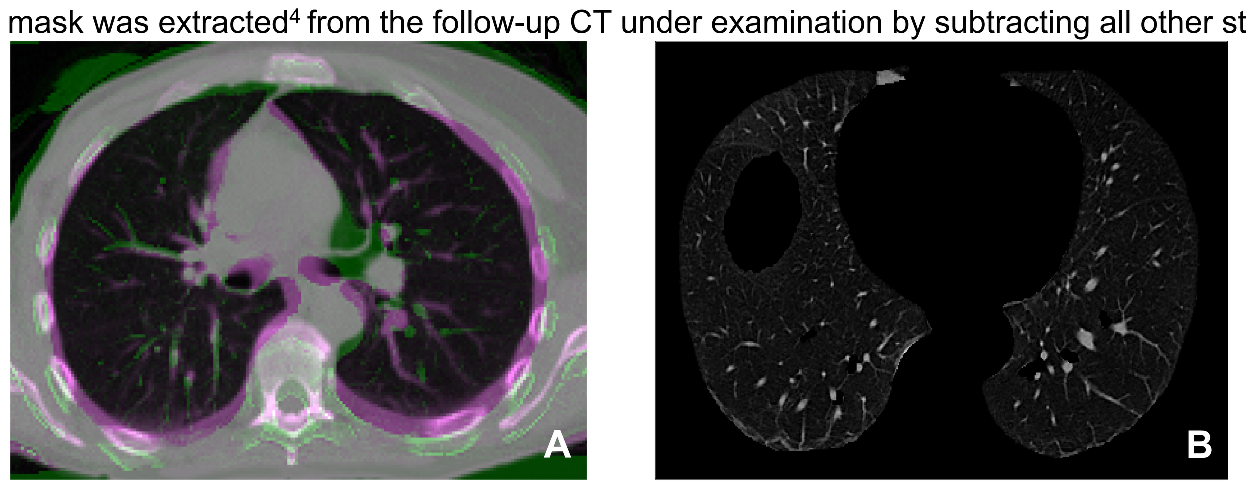

Figure 2. Image Registration and Lung-mask Extraction: [A] illustrates the axial view of the registered image set. The objective is to register the green (follow-up) image to the purple (planning CT). [B] is the resultant lung-only volume after subtracting other structures from the axial lung CT dataset under examination.

AIRWAY AND VESSEL MASK EXTRACTION

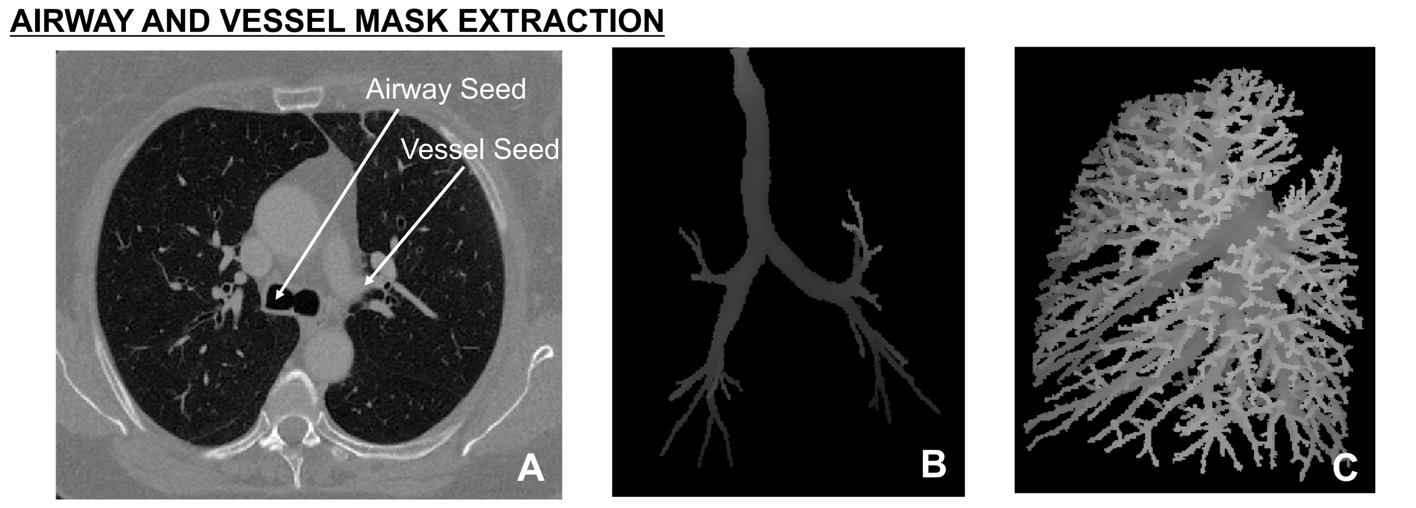

Figure 3. Airway and Vessel mask extraction: This step is intended to subtract airways and vessels from the lung volume mask to preserve just the lung tissues. [A] is a representative slice from a lung CT dataset. [B] and [C] are the depth-enhanced MIP (maximum intensity projection) of the extracted airway and vessel-tree using seeded region growing and a Fast-Marching[5] approach respectively. A seed corresponding to an airway and a vessel is initialized (shown in [A]) and is used to segment the airways and the vessel tree

COMPUTING FOLLOW-UP LUNG TISSUE-DOSE RESPONSE

- **Visual grading:** Radiation induced lung injury (RILI) was graded 0-3 as per Lind *et al.*[6]: Grade 0: no change; Grade 1: low opacity in linear streaks; Grade 2: moderate opacity; Grade 3: complete opacity. Grading was performed by an investigator blinded to the treatment modality.
- **CT-based tissue damage analysis:**

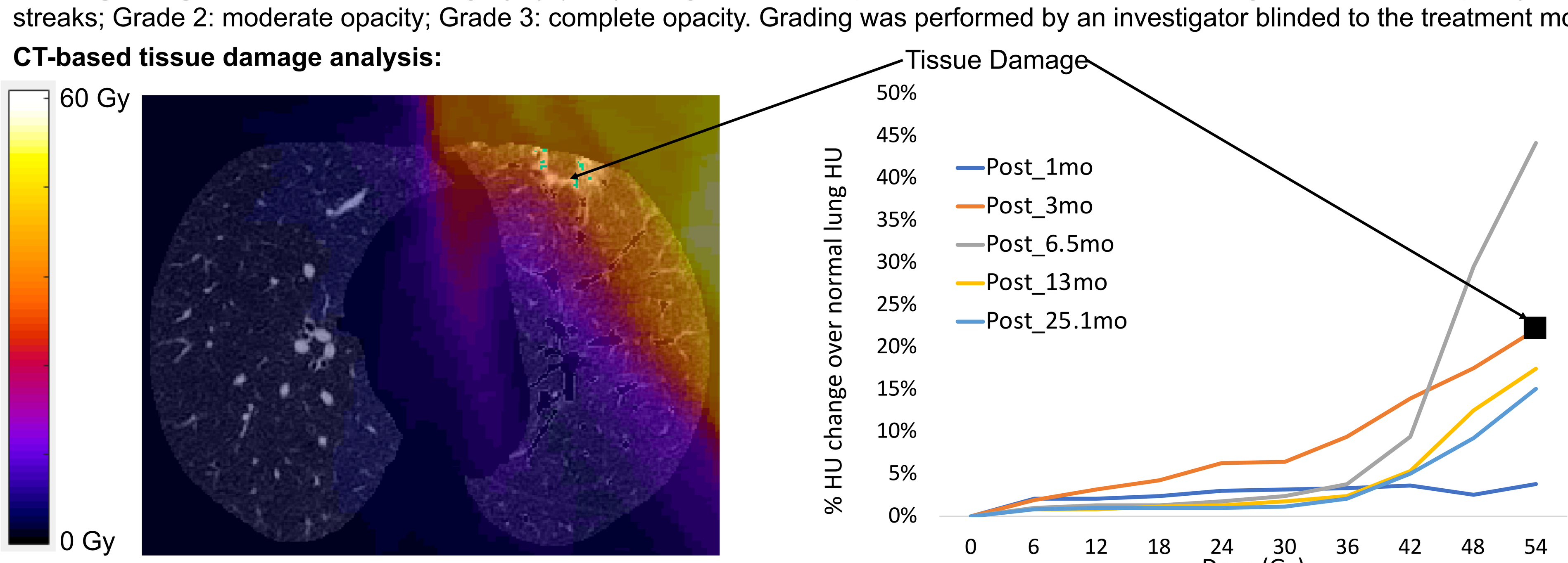

Figure 4. **Lung tissue dose response:** Dose was warped from planning to follow-up CT. The color scheme goes from black (0 Gy) to white (the maximum dose in Gy, typically 50–60 Gy); Lung tissue response in % Hounsfield units (HU) change over normal lung HU as a function of the dose exposed at various time-points post radiation was computed; CT based tissue damage was reported as maximum % HU change (tissue-density enhancement), typically occurring at high dose regions (40-60 Gy).

III. RESULTS

DOSE VOLUME HISTOGRAM (DVH) AND V20 ANALYSIS: PROTON THERAPY (PT) VS. PHOTON THERAPY (XRT)

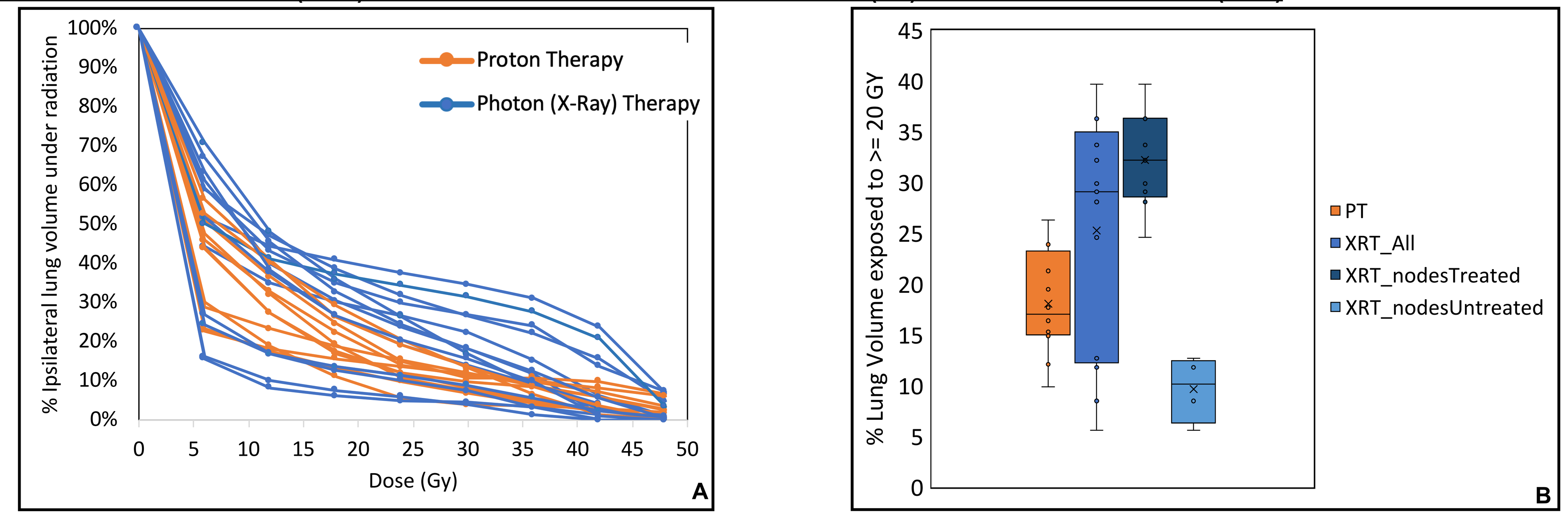

Figure 5. **DVH and V20 - PT vs. XRT:** [A] Of the 25 patients, 12 were treated with PT (orange curves) and 13 with XRT (blue). 4 XRT patients did not receive regional nodal irradiation, resulting in lower lung dose (4 lowest blue curves). [B] shows quartile plots of volume of the ipsilateral lung receiving >20 Gy (V20) with the vertical bars indicating range. The V20 was 18.1% (Range: 9.9%-26.3%) with PT and 25.3% (Range: 5.6%-39.7%) with XRT. V20 for those XRT without nodal irradiation was 9.6% (5.6%-12.7%) and with nodal irradiation was 32.2% (24.6%-39.7%).

PNEUMONITIS GRADING AND CT-BASED TISSUE DAMAGE QUANTIFICATION- 6 AND 12 MONTHS POST-RT

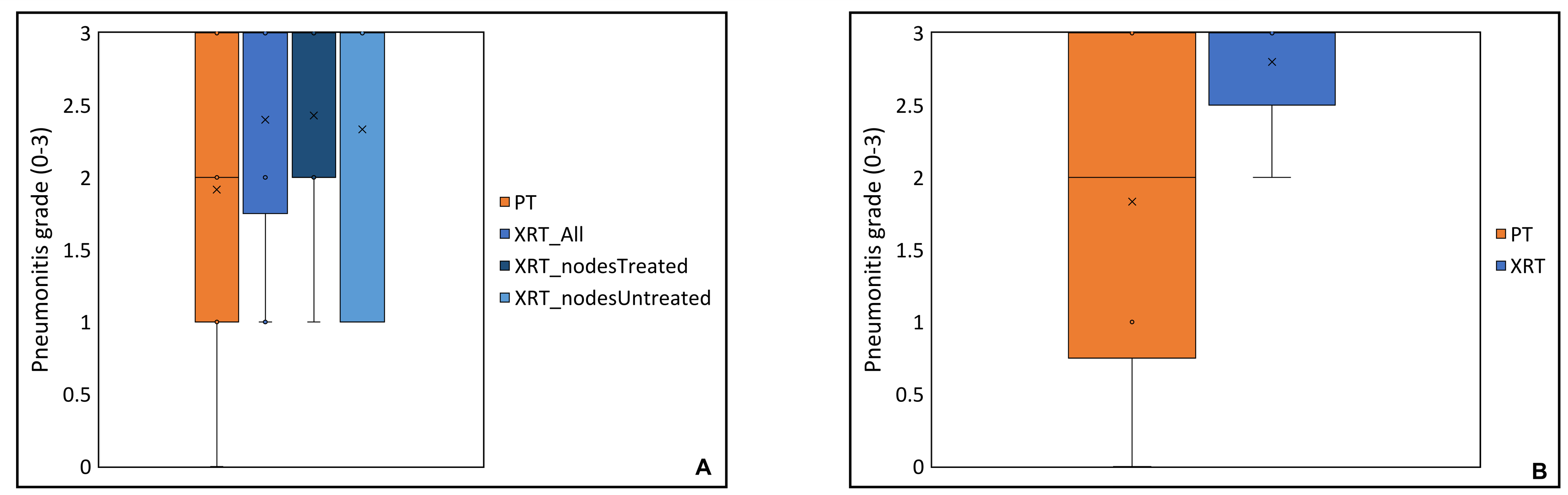

Figure 6. **Incidence of Pneumonitis (Visual grading) :** [A] The incidences of the grade 2-3 RILI at 6 months post-RT were 58.3% (7 of 12 patients) and 80% (8 of 10 patients), for PT versus XRT treatment, respectively. Of the 10 photon patients, 3 did not receive nodal RT. [B] At 1 year, 50% (3 of 6) of PT patients and 100% (5 of 5) of XRT patients presented with grade 2-3 RILI. To-date, no XRT patient without nodal treatment provided 1-year data.

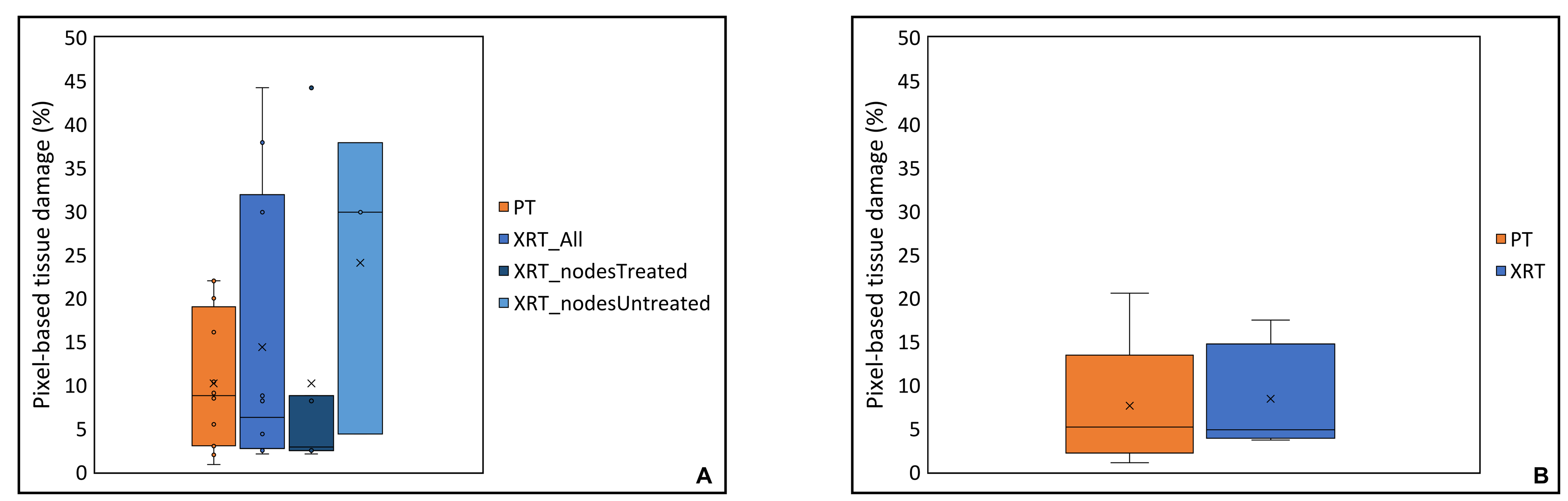

Figure 7. CT-based tissue damage analysis: CT based tissue damage was quantified using maximum mean pixel-intensity tissue enhancement over background lung tissue. A mean tissue damage of [A] 10.2% (12 patients; 0.9%-16.1%) and 14.4% (10 patients; 2.1%-44.2%) at 6 months and [B] 7.6% (6 patients; 1.1%-20.6%) and 8.4% (5 patients; 3.7%-17.5%) respectively, among patients treated with PT vs. XRT.

IV. CONCLUSIONS & DISCUSSION

- For patients receiving treatment to the lymph nodes, V20 and DVH are lower for PT versus XRT. XRT patients without nodal treatment tended to have lower V20 and DVH than PT and XRT patients with nodes treated.
- Asymptomatic grade 2-3 RILI appeared to scale with V20, with PT patients tending to have a lower incidence of toxicity.
- Ongoing analysis will address key clinical questions such as:
  - Does PT improve the therapeutic ratio of breast cancer radiation treatment by reducing the severity of radiation toxicity to the lungs?
  - Can we identify breast cancer survivors that are at an elevated risk for lung toxicity who may benefit from proton therapy or altered RT?
  - Is there a role for routine imaging in clinical follow-up care of breast cancer patients for identification of early symptoms of lung toxicity?

V. REFERENCES

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