MLS analysis of INSIDE in-beam PET images for the detection of morphological changes in patients treated with protontherapy

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Introduction

- Anatomical changes occurring during proton therapy treatment are considered a relevant source of uncertainty in delivered dose.
- The INSIDE in-beam Positron Emission Tomography scanner, installed at the National Oncological Center of Hadrontherapy (CNAO), performs in-vivo range monitoring to obtain information about morphological changes in the irradiated tissue.
- Our purpose is to assess the sensitivity of the INSIDE PET system in detecting anatomical changes using inter-fractional range variations methods.
- This study is based on MC simulation and real data of proton treated patients at CNAO (ID: NCT03662373).

Materials and Methods

Data: MC simulation of in beam PET (IB-PET) data of gradual emptying of the nasal cavity. IB-PET data of eight patients treated with proton therapy at CNAO. Two patients had shown morphological changes (Fig. 1).

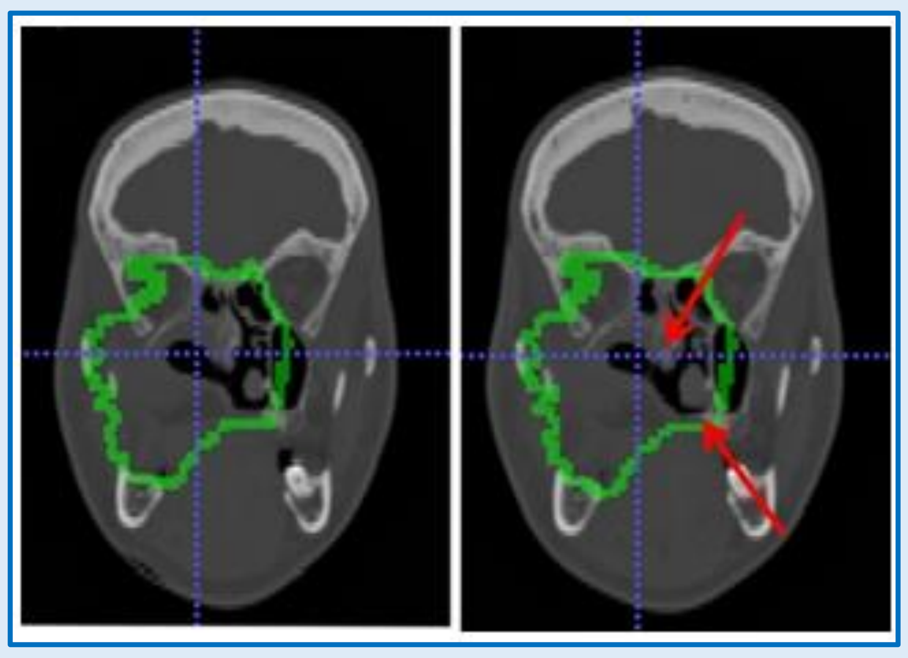

Figure 1: Coronal view of the planning CT (left) and control CT (right) for patient 007P. The morphological change is highlighted with a red arrows and the CTV (Clinical Target Volume) area is highlighted with a green line.

PET system: dual head INSIDE PET system installed at CNAO[2].

The proposed inter-fractional range variation analysis consists of:

- Analyzing the profiles along the beam axis, in the distal fall off area, using for the first time to IB-PET data, the **Most-Likely-Shift (MLS) method**[3]. To establish the efficacy of the MLS method, is introduced the **Beam's Eye View (BEV) method**[4].
- A distribution of all range differences values $\delta_{MLS}(x,y)$ and $\delta_{BEV}(x,y)$ was created for each fraction of treatment compared respect to the reference image M (Fig. 2). The **reference image** was calculated as the **average of the first two monitored fractions**.

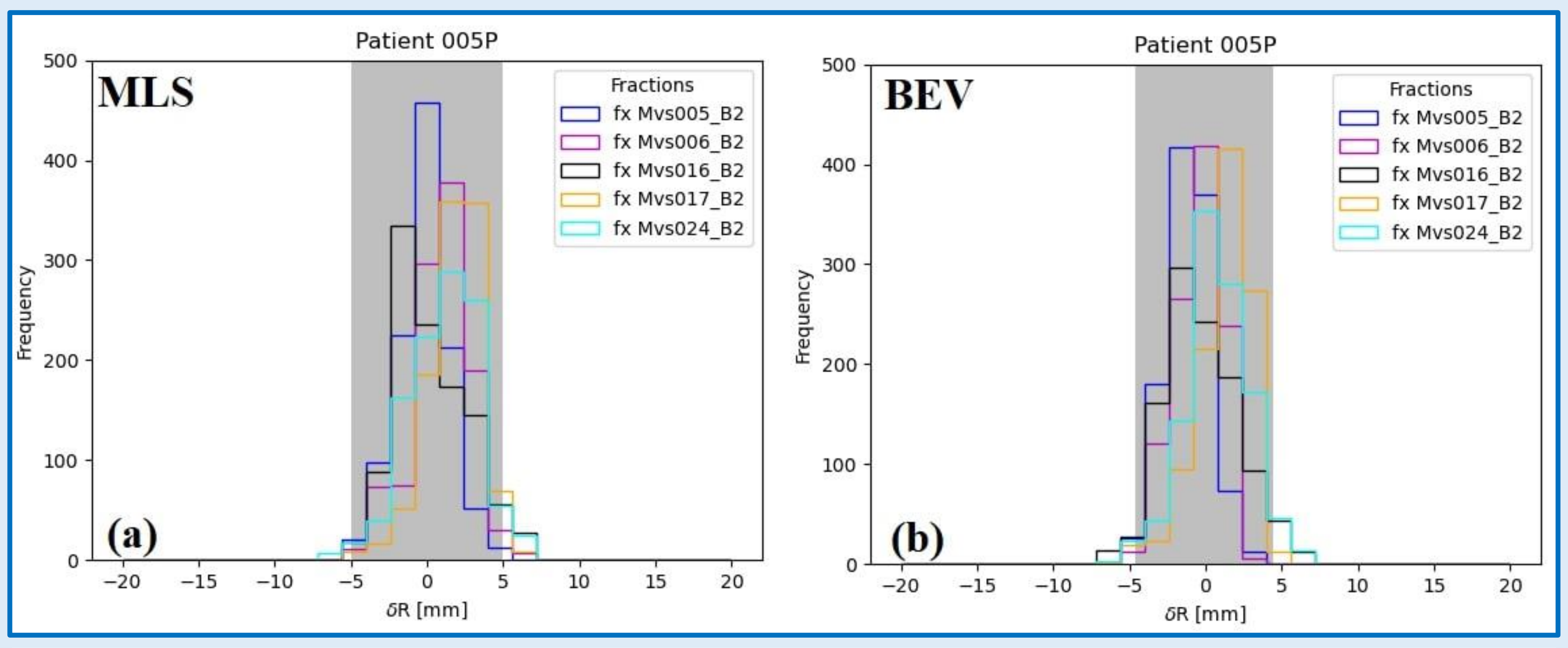

Figure 2: Examples of the distributions of inter-fractional range differences δR(x, y) of various fractions with respect to the reference (M) in patient 005P for the MLS method (a) and the BEV method (b).

- To investigate the level of fluctuations in our PET data in absence of any morphological changes, we extracted for the six patients without any morphological changes the average standard deviation Σ.
- For each patient and each analysed fractions, a three-dimensional outliers map $O_{MLS/BEV}(x,y,z)$ of anomalously large shifts was created in order to visualise the largest range difference obtained.

Results

- For patients not subject to anatomical changes (squares in Fig. 3) Σ was found to be 2.5 mm with the MLS method and 2.3 mm with the BEV method. For the two patients where small anatomical changes occurred, we found larger standard deviation values.

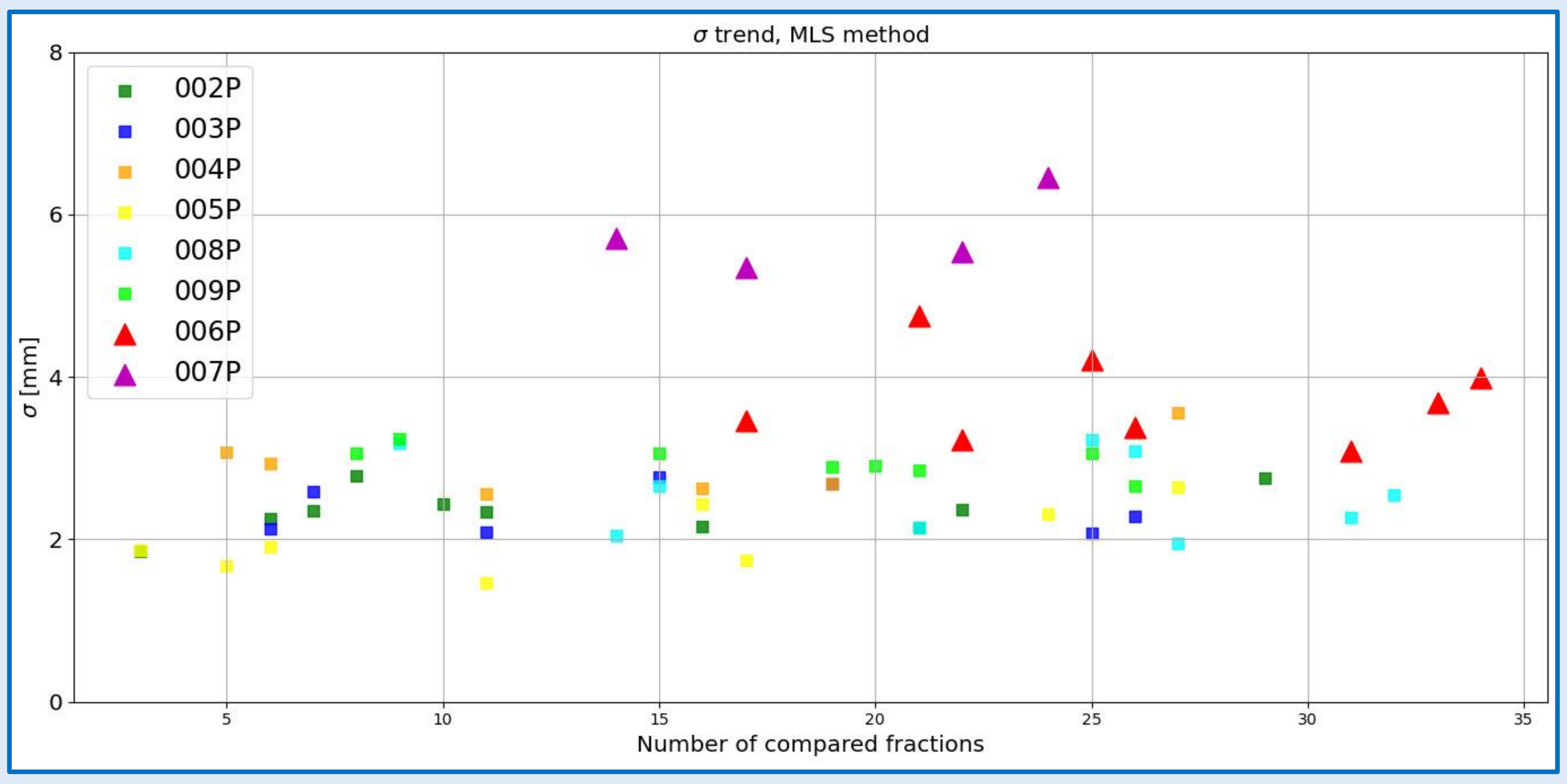

Figure 3: Inter-fractional standard deviation of the range difference distribution $\delta_{MLS}(x,y)$. The triangles stand for the patients that changed, while the squares represent the patients that did not showed changes.

- In the simulated patient case, the standard deviation gradually increases according to the increasing anatomical changes.
- The changes detected with our range analysis were localized in the same zones as the one observed with the control CT scans (Fig. 4).

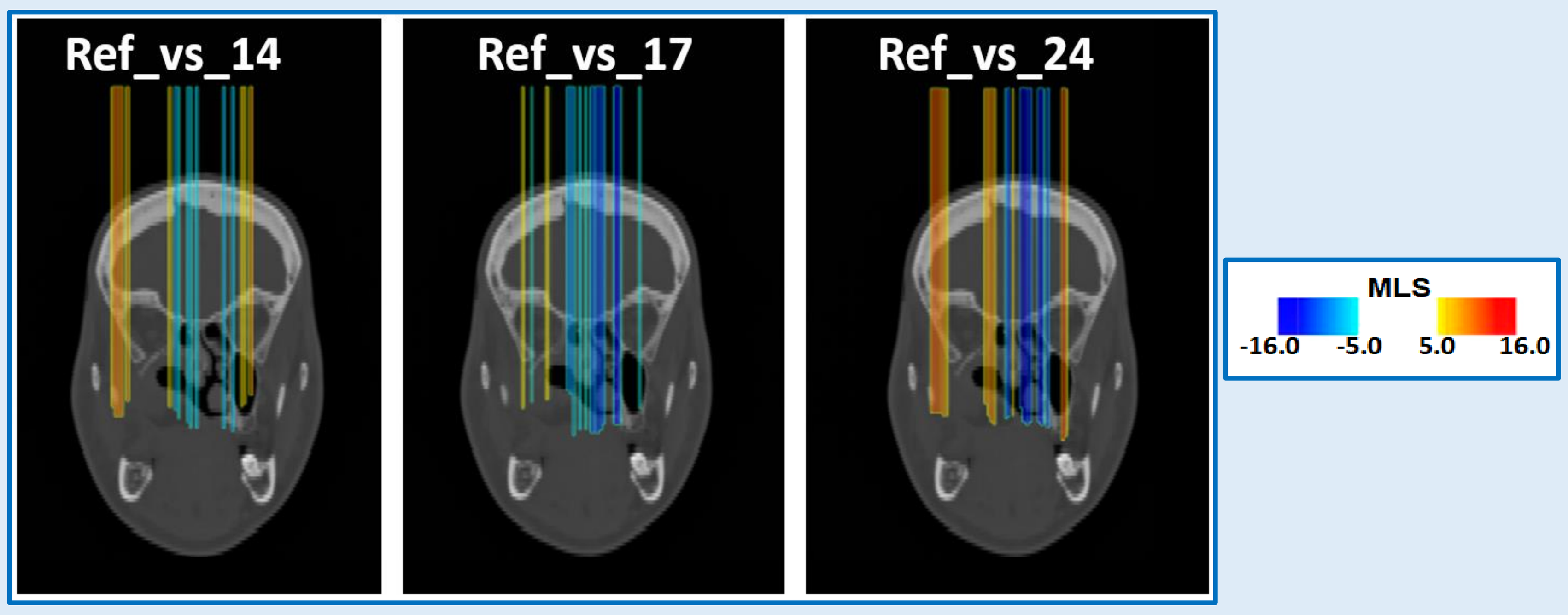

Figure 4: Coronal views of the control CT of patient 007P, with superimposed the MLS outliers map obtained. Red and blue indicating a range overshoot and undershoot with respect to the initial situation, respectively.

Conclusions

- **Outliers maps indicate anomalous range variations**. These regions covered those **with real anatomical variations observed in the control CT**.
- The MLS method is an encouraging tool to correctly **identify regions with morphological changes both in simulations and real data**.
- Both MLS and BEV can possibly be used as a **support tool by clinical personnel to detect anomalous situations during the treatment** course and to guarantee the effectiveness of the treatment plan.

References

[1] W. Enghardt et al., *Charged hadron tumor therapy monitoring by means of PET*, Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment 525.1, 2004

[2] G. M. Bisogni et al., *INSIDE in-beam positron emission tomography system for particle range monitoring in hadrontherapy*, Journal of Medical Imaging 4, 2016

[3] Frey K, et al. *Automation and uncertainty analysis of a method for in-vivo range verification in particle therapy*. Physics in Medicine & Biology (2014).

[4] E. Fiorina et al., *Detection of Interfractional Morphological Changes in Proton Therapy: A Simulation and In Vivo Study With the INSIDE In-Beam PET*, Frontiers in Physics 8, 2021.