

**ion 2025
imaging
workshop**

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In vivo treatment verification in head and neck tumors using secondary fragments in ^{12}C ion therapy

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on behalf of the INSIDE collaboration

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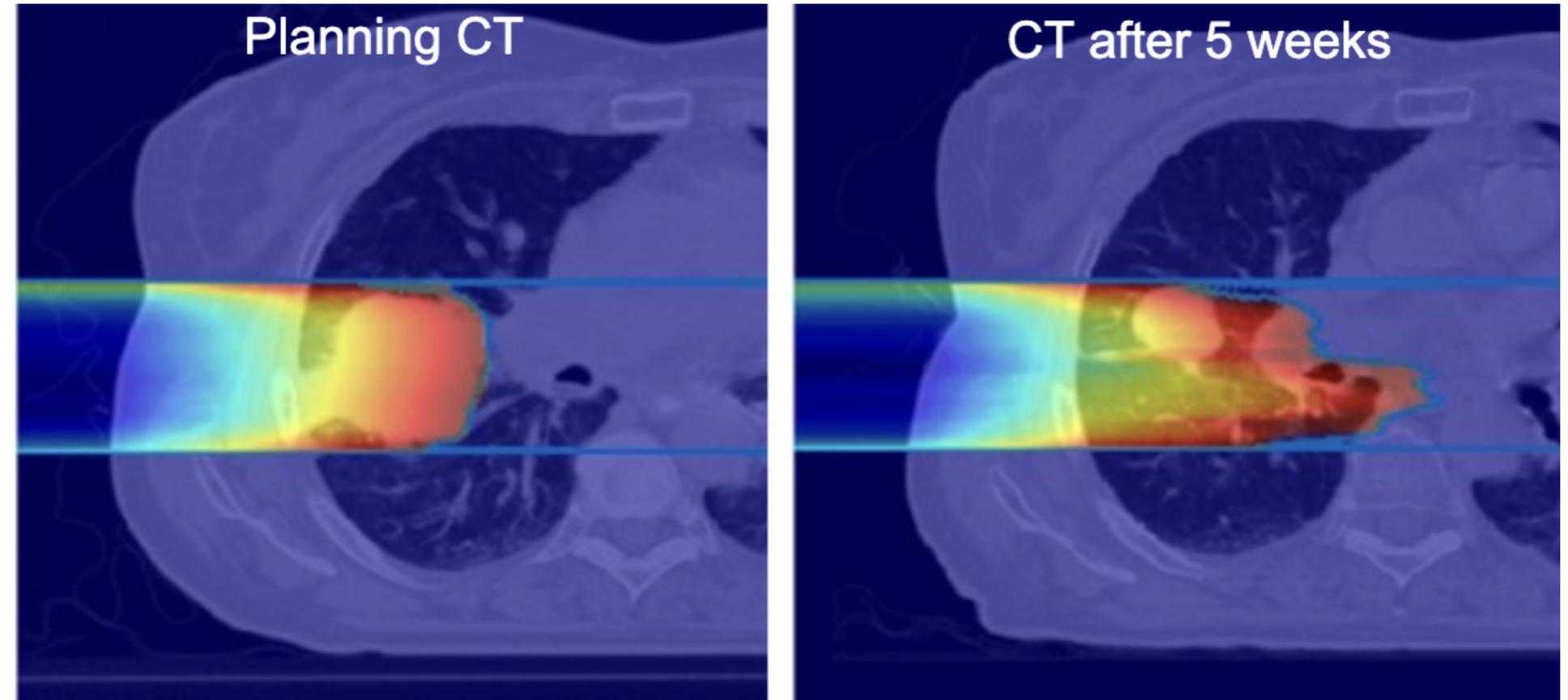
Treatments in vivo-verification: motivations

Future direction of particle therapy, Tony Lomax, Oxford 2008

- The dose delivered to the patient is strongly affected by range uncertainties:

- ▣ Relative Stopping Power (RSP) (with respect to water) \leftrightarrow **HU conversion**. Today based on Schneider-Parodi conversion doi: 10.1118/1.1833041.

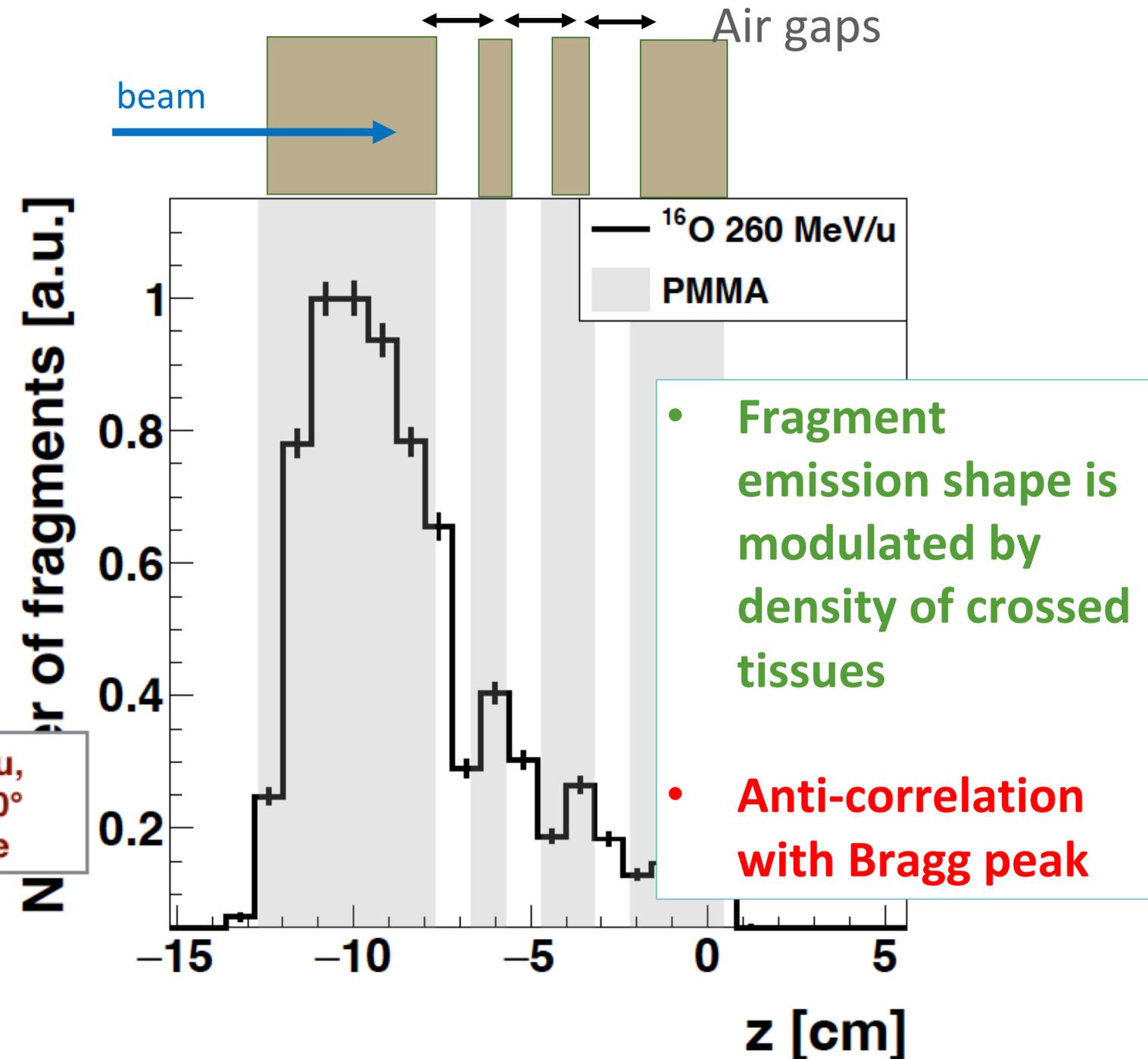
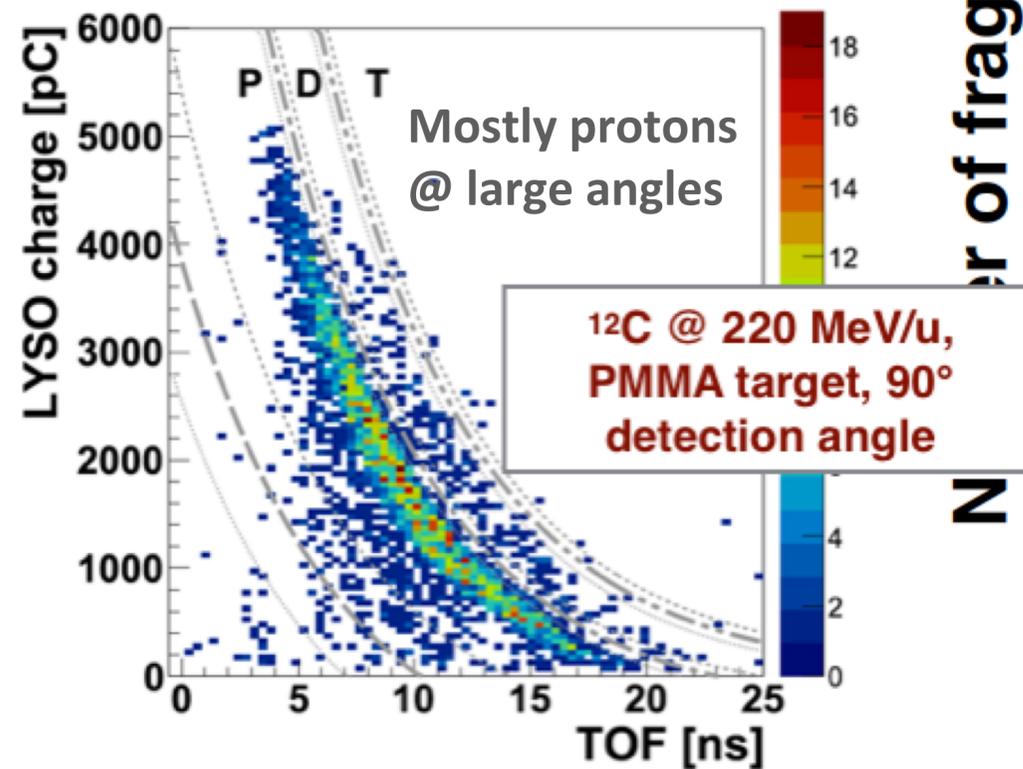
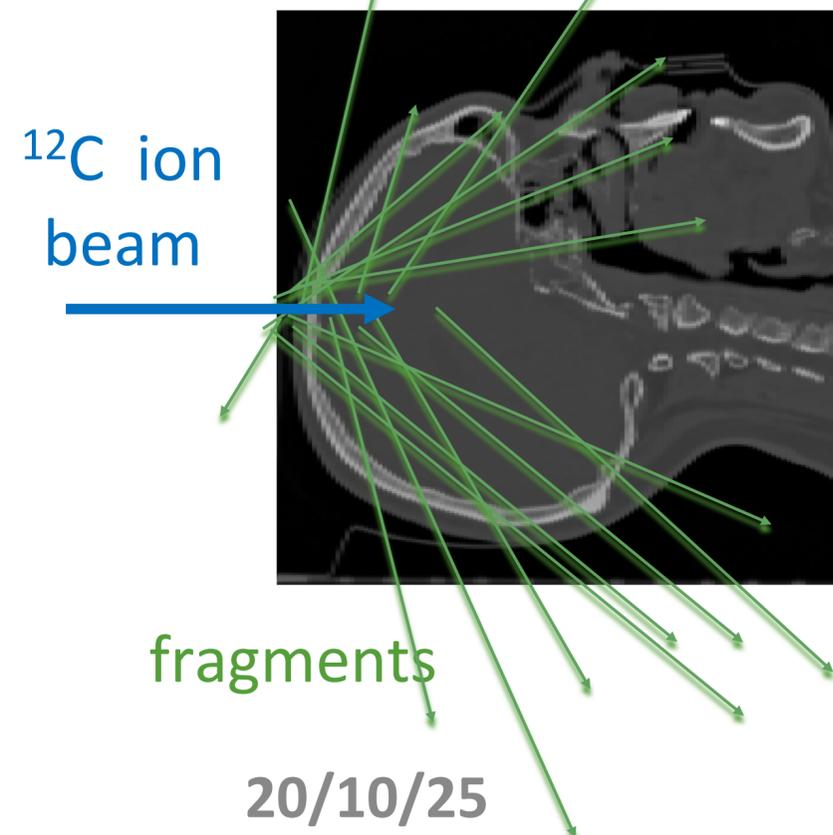
- ▣ Morphology changes (inter-fraction, mis-alignment, breath-induced movement)



There is no system capable of taking account to that!

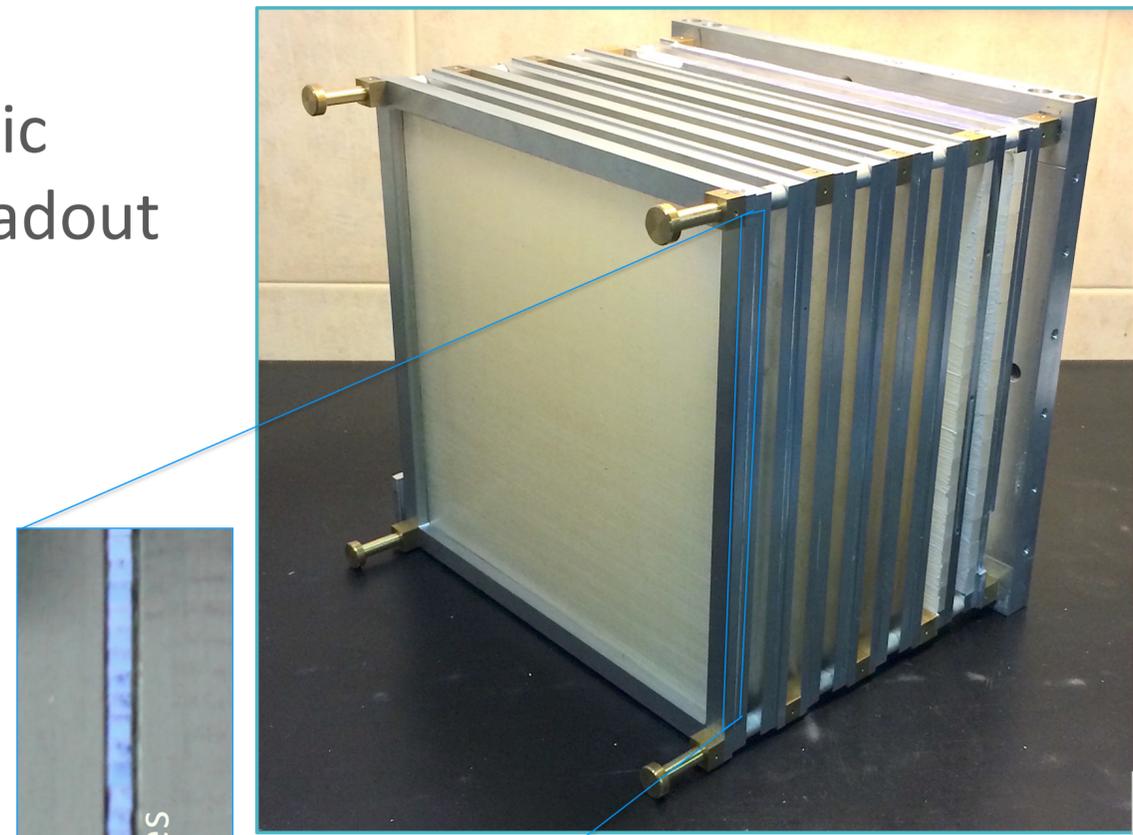
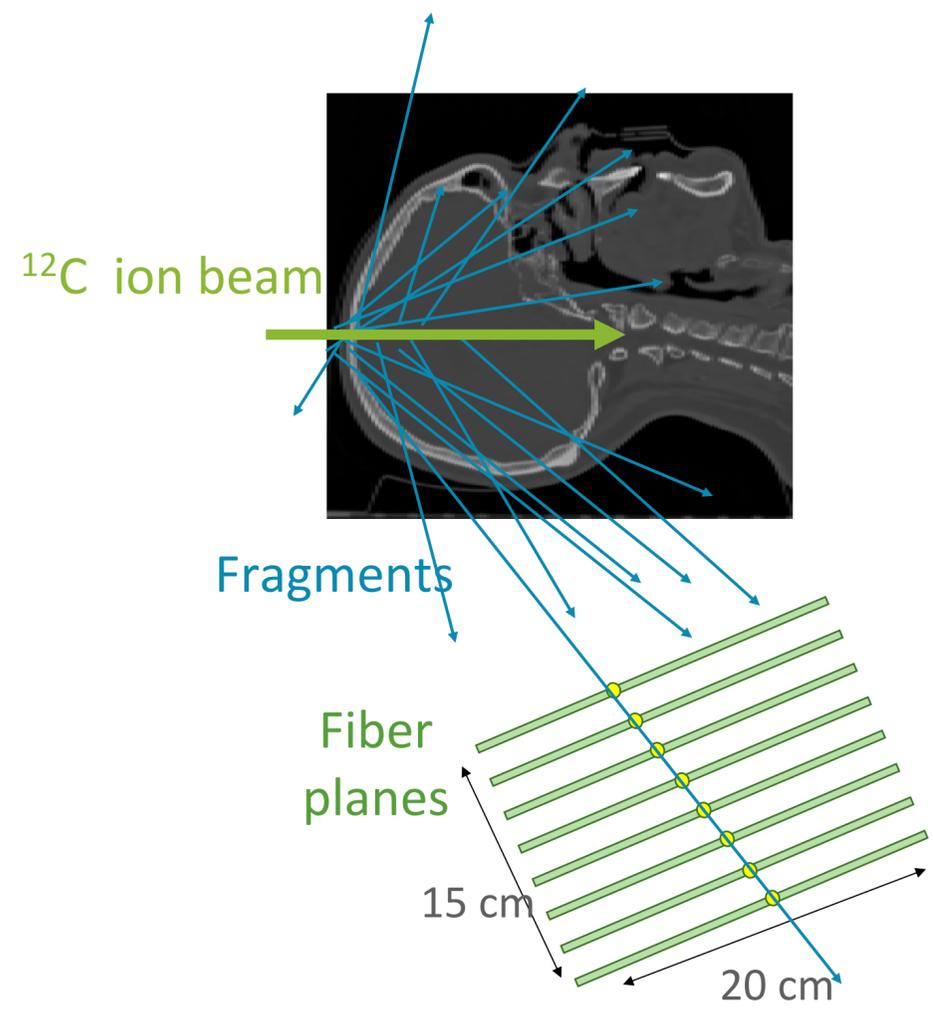
Exploiting charged secondary fragments @ large angle

- Significant emission in $Z > 1$ ion treatments
- Easy to detect with high efficiency
- Large angle detection needed to avoid for spoiling spatial resolution (trade-off with collectable statistic is crucial)
- Resolution limited by Multiple Scattering

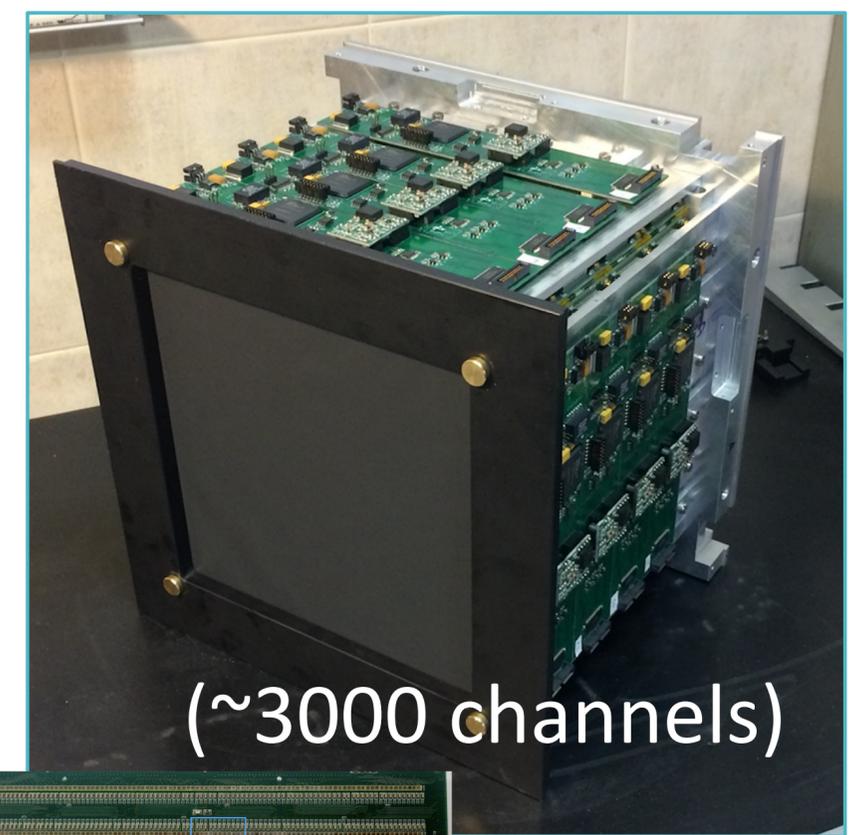


The detector: Dose Profiler

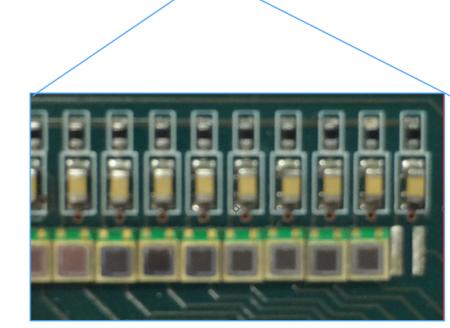
8 planes each one composed of 2 orthogonally oriented layers of plastic **scintillating fibres** (500 μm thick) readout by **SiPMs** (1 mm^2)



Saint-Gobain (BFC-12), 500 μm^2



(~3000 channels)



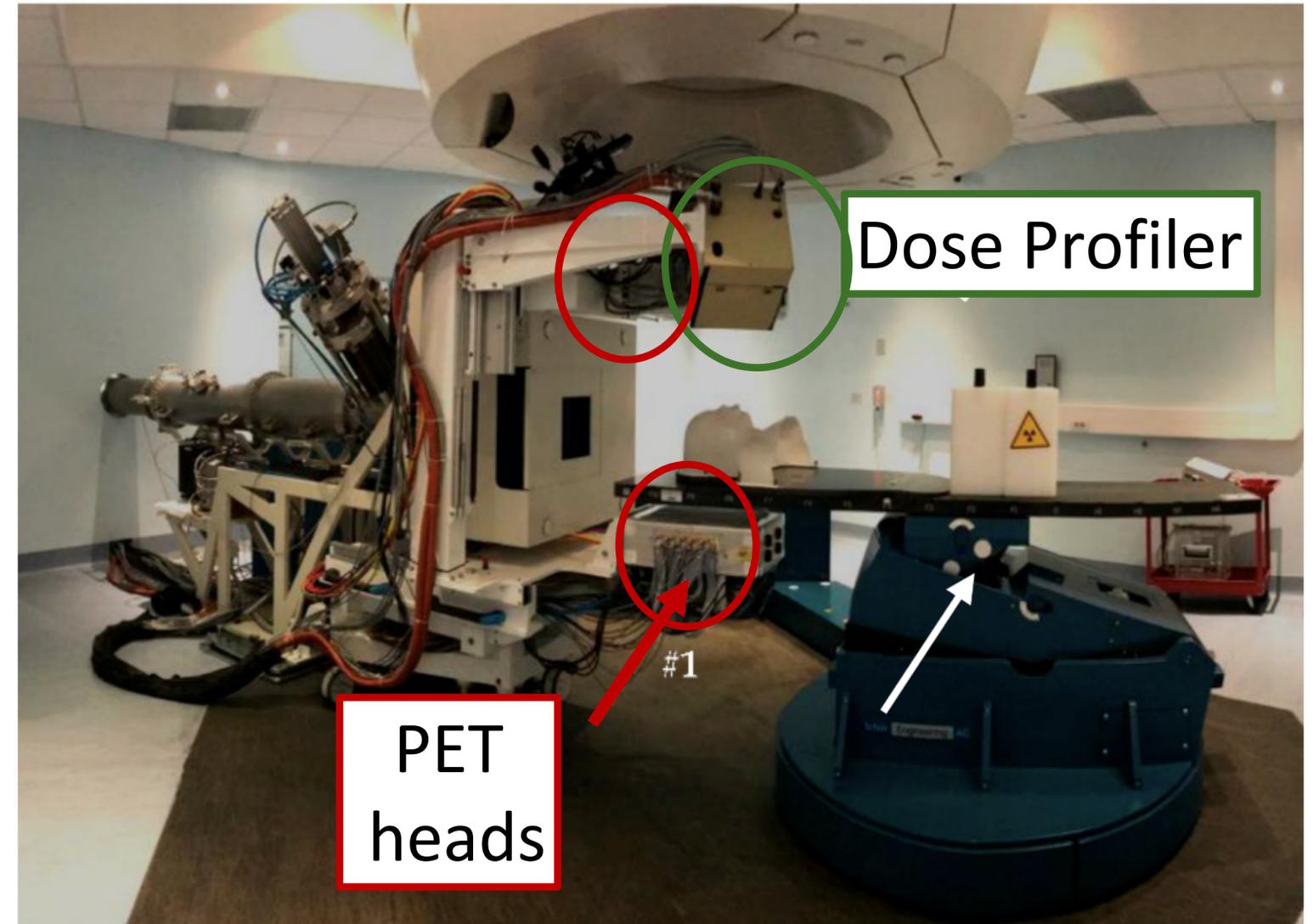
SiPM 1 mm^2 Hamamatsu



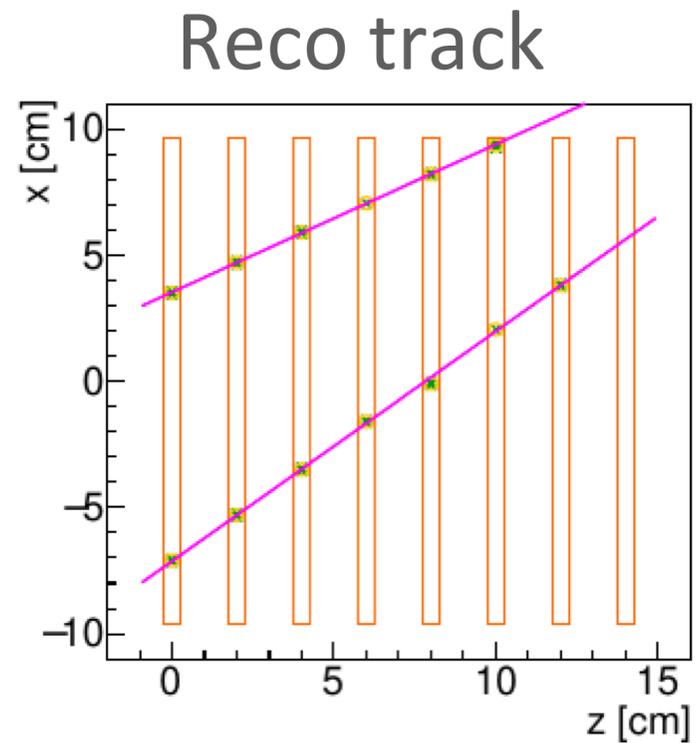
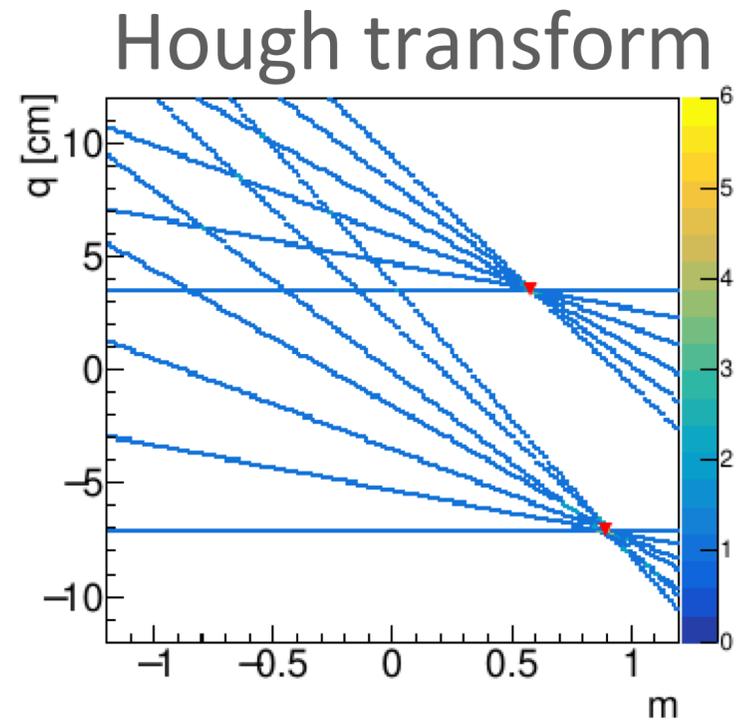
INSIDE (Innovative Solutions for Dosimetry in Hadrontherapy)

The DP is integrated within the INSIDE system
@CNAO with a PET device (see the next talk of F.Pennazio).

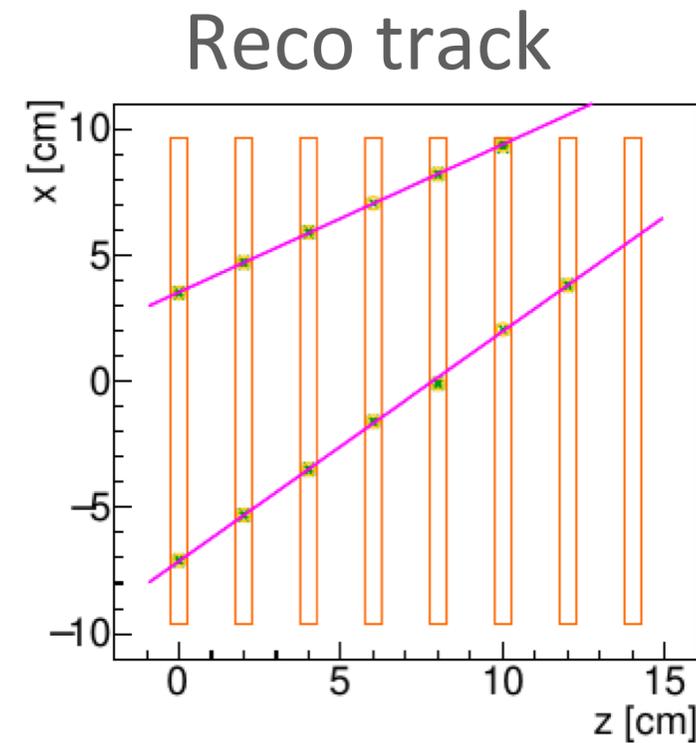
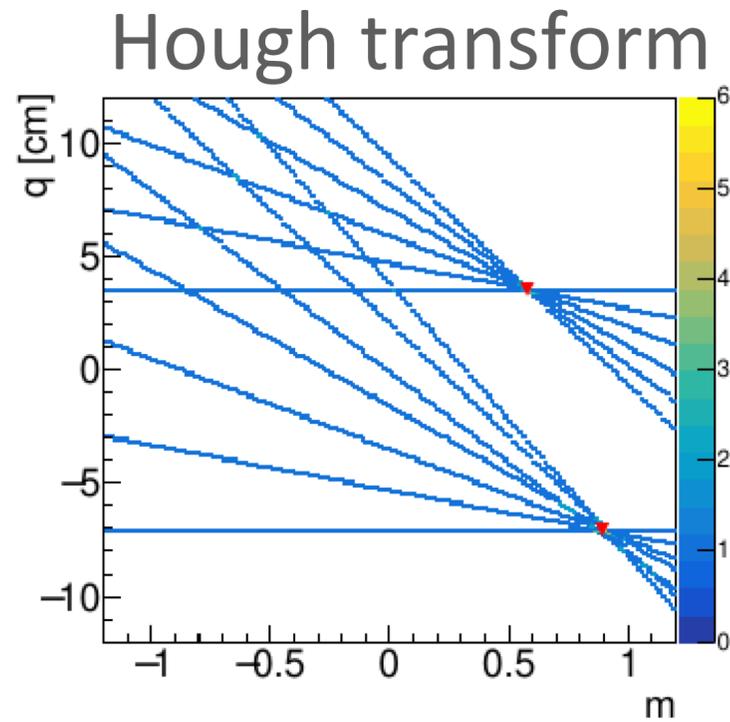
- INSIDE pioneered the **bi-modal approach** with synergistic combination of PET and charged fragment detection.
- In beam PET exploits the β^+ emitters activated by the beam inside the patient (^{11}C , ^{10}C , ^{14}O , ^{15}O , ^{13}N ...). It's more suitable for proton treatment monitoring
- Charged fragments emission significantly occurs only in ^{12}C treatment.



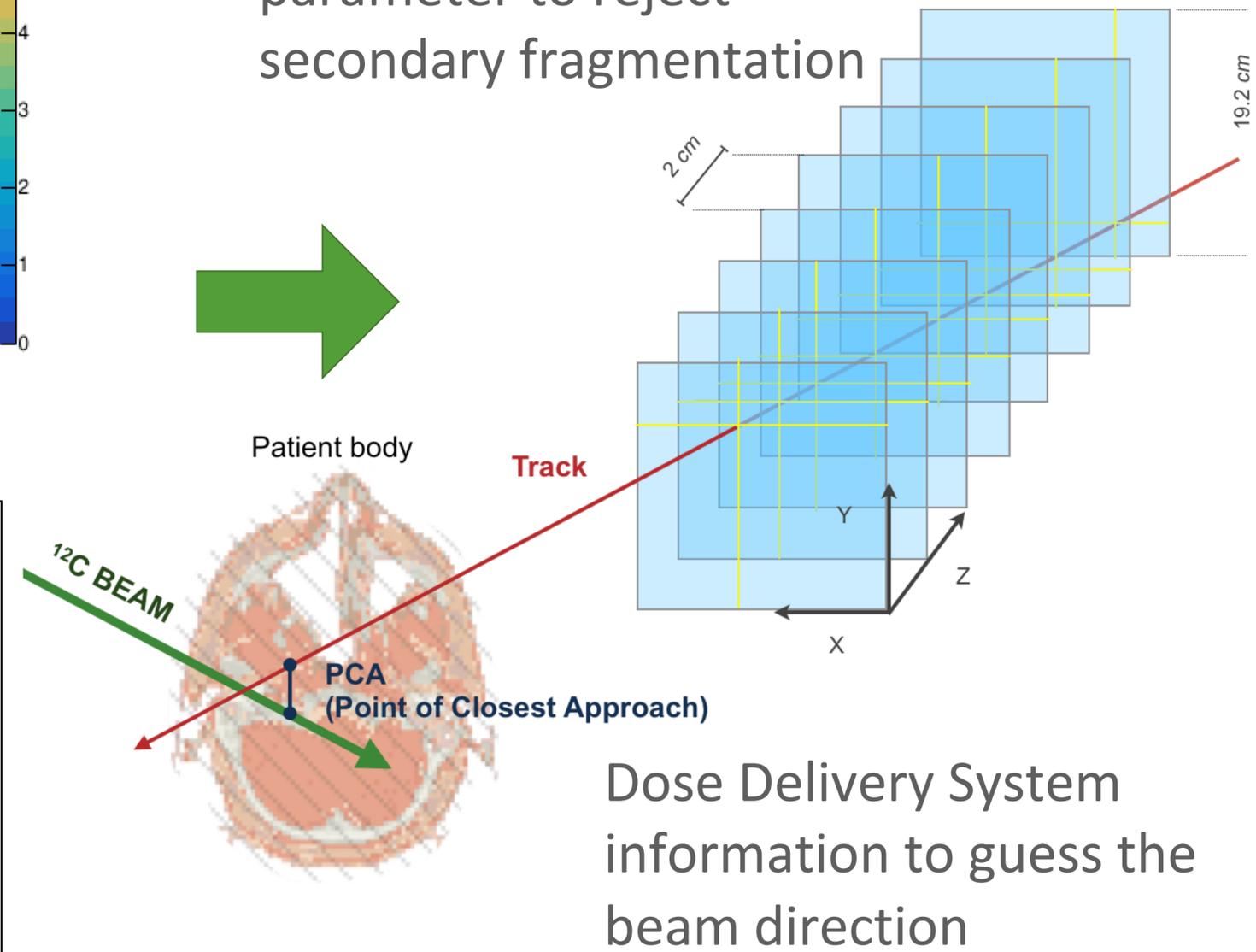
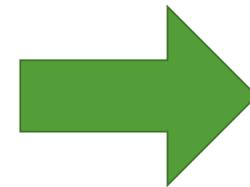
Secondary fragments detection and 3D map reconstruction



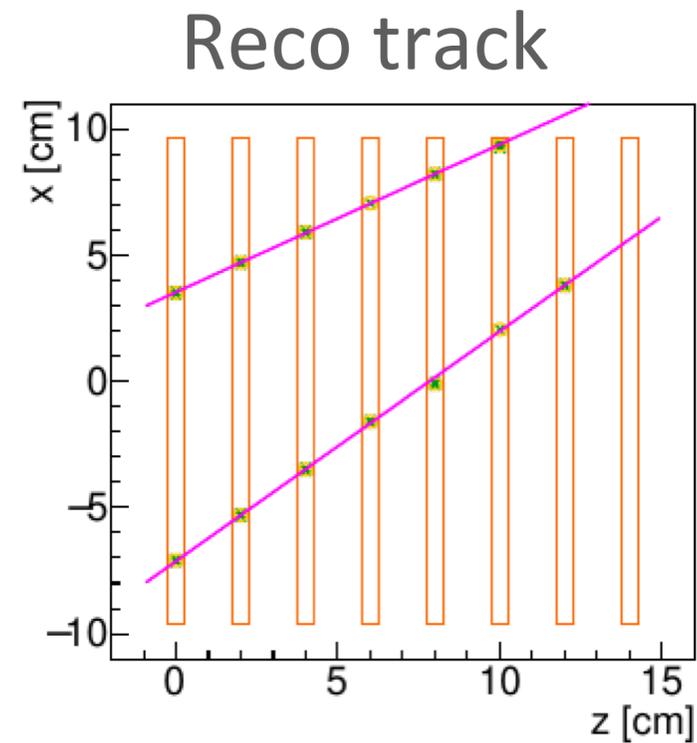
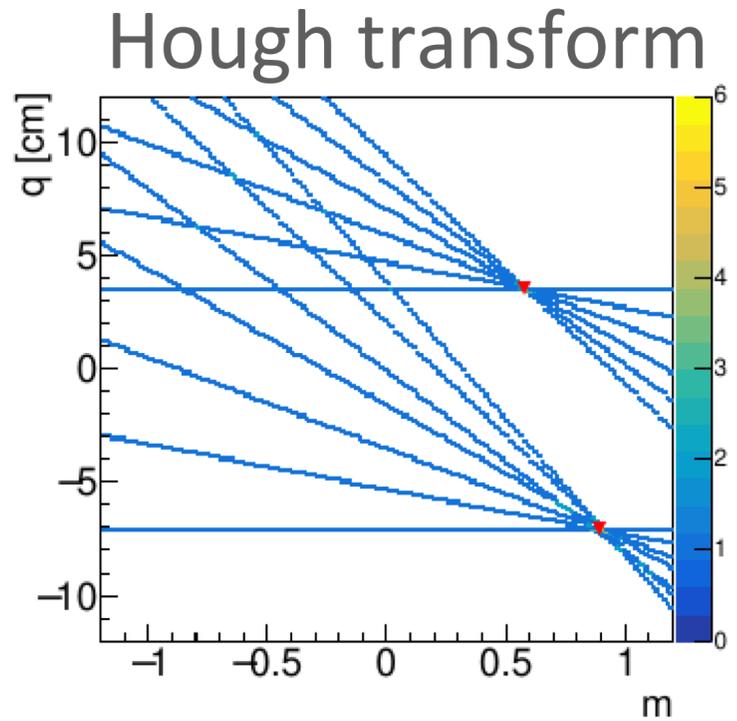
Secondary fragments detection and 3D map reconstruction



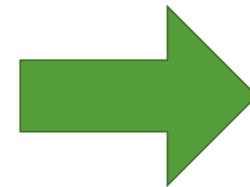
Selection on impact parameter to reject secondary fragmentation



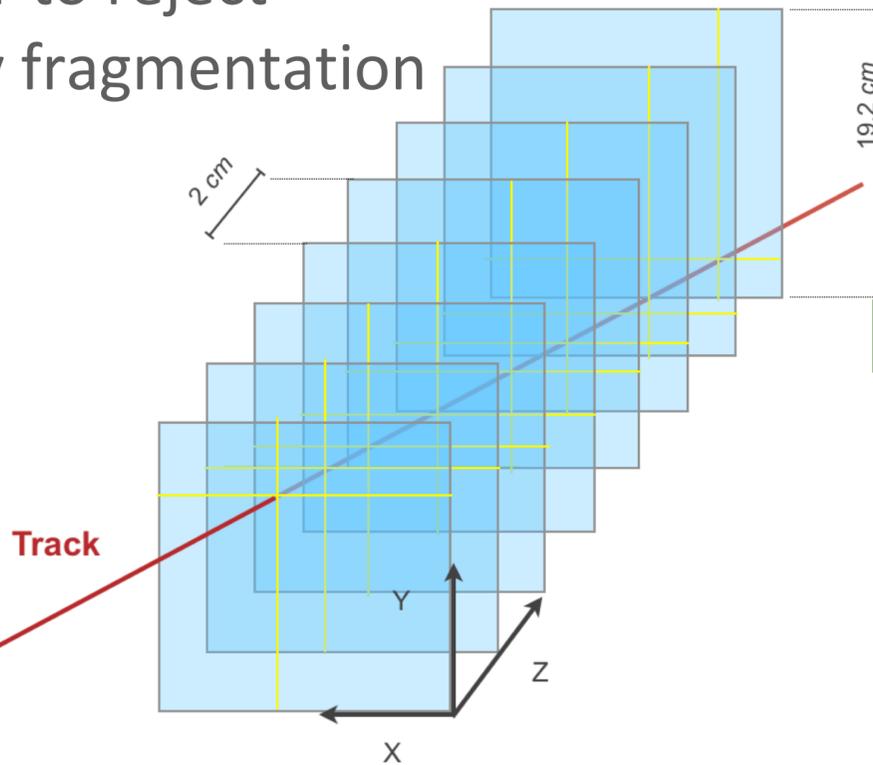
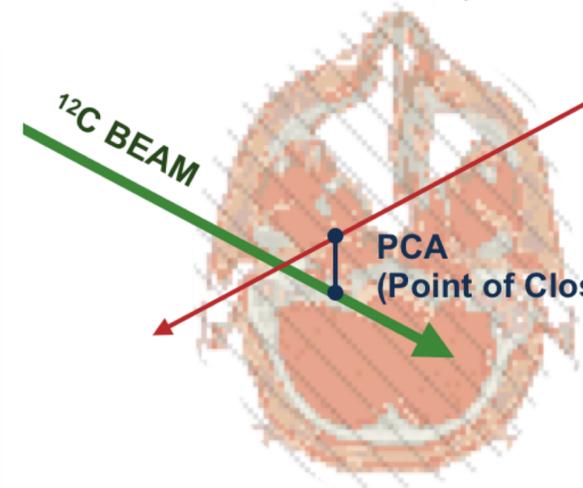
Secondary fragments detection and 3D map reconstruction



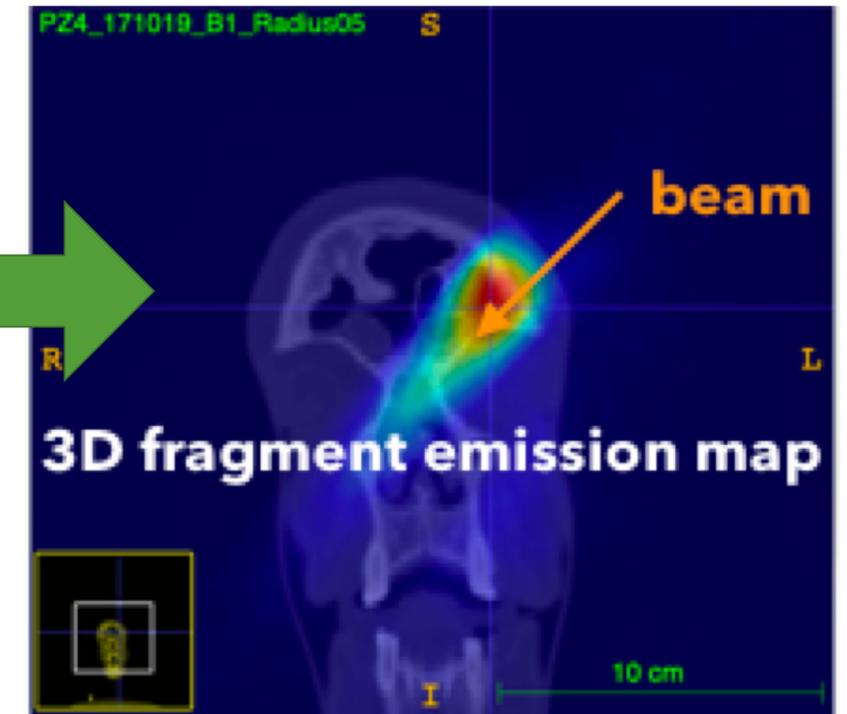
Selection on impact parameter to reject secondary fragmentation



Patient body

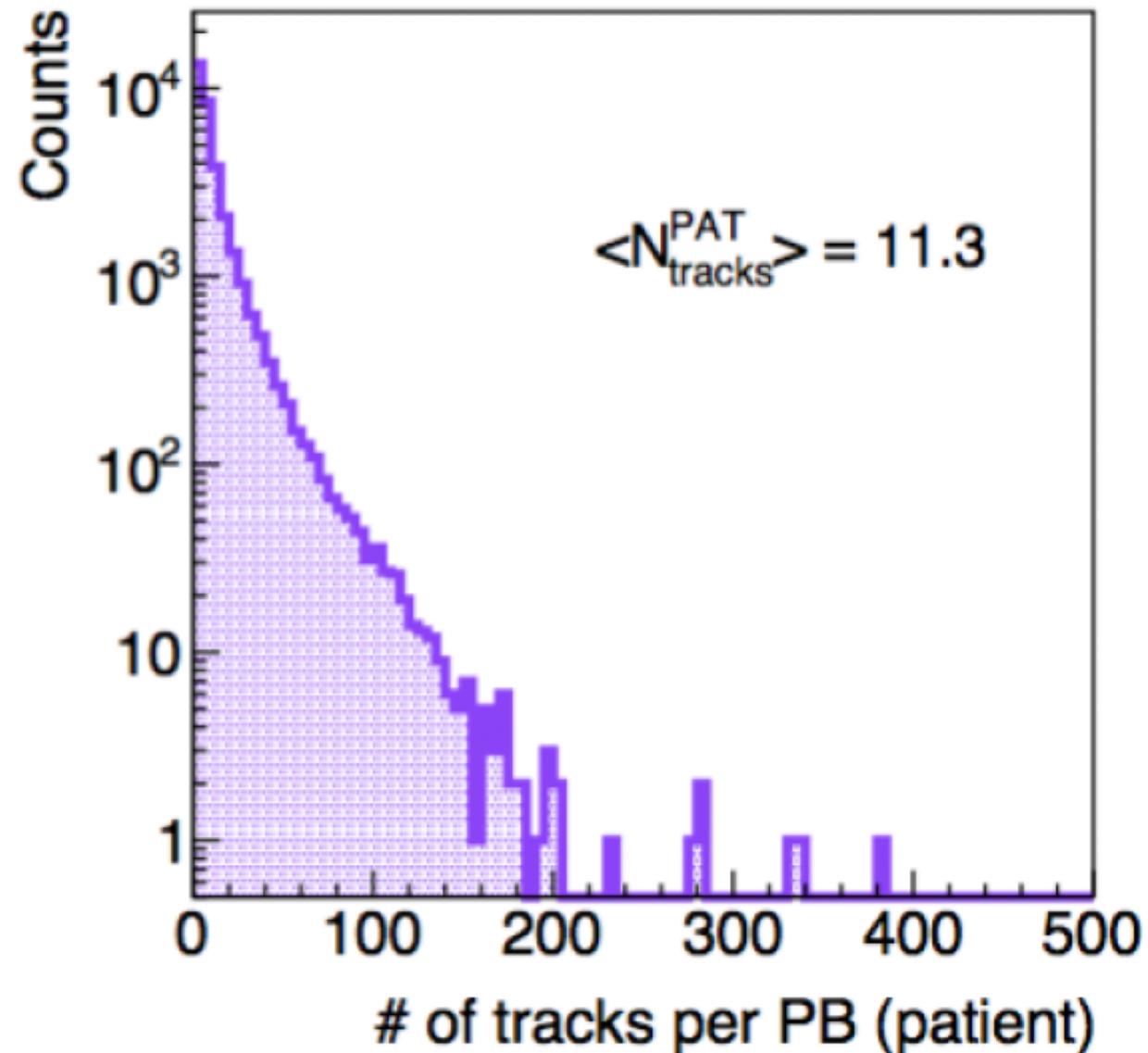


Dose Delivery System information to guess the beam direction

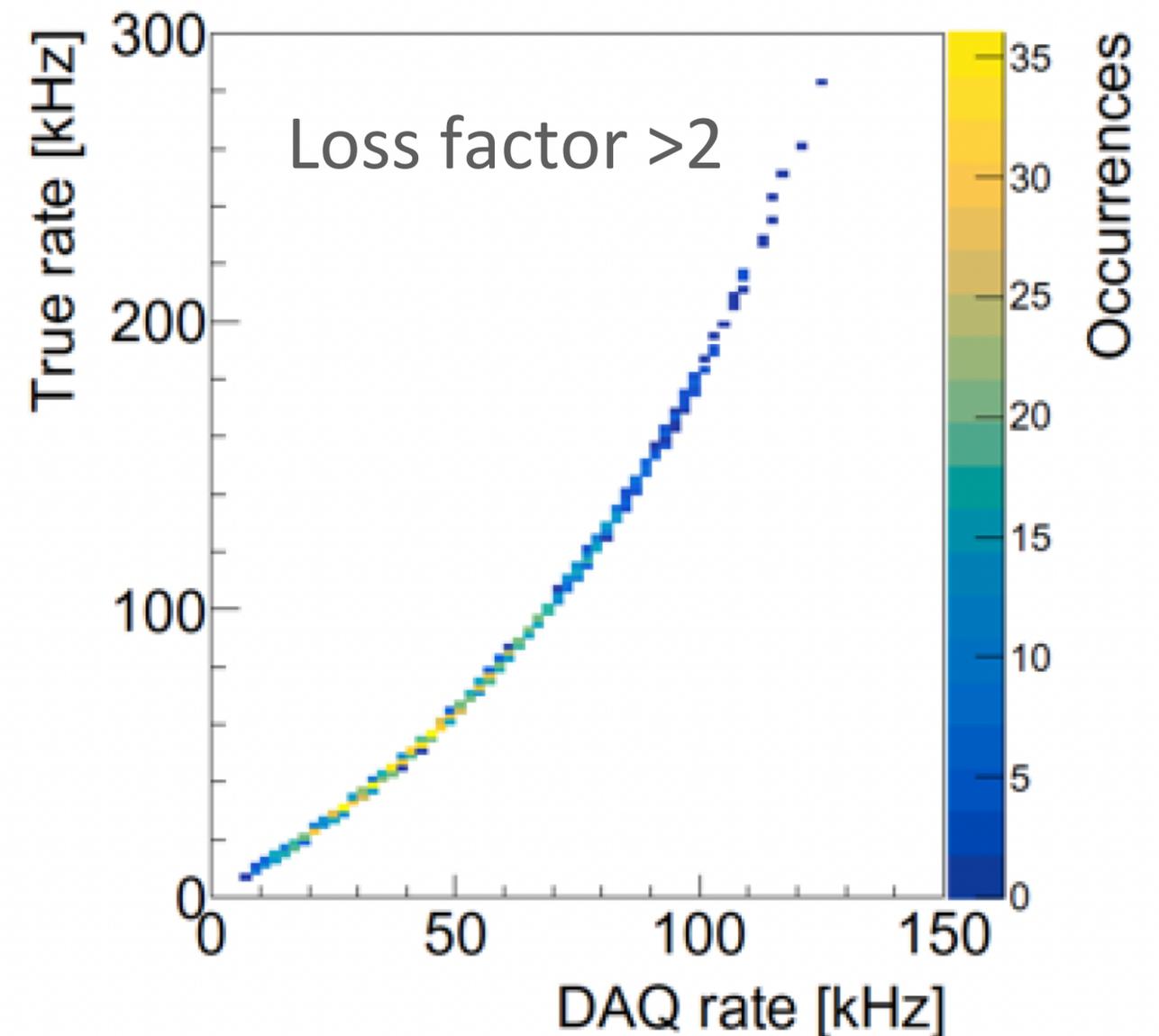


Critical issues

Low statistics (1-2M fragments/fraction),
few particles per PB, (max) ~ 10000
particles/cm³



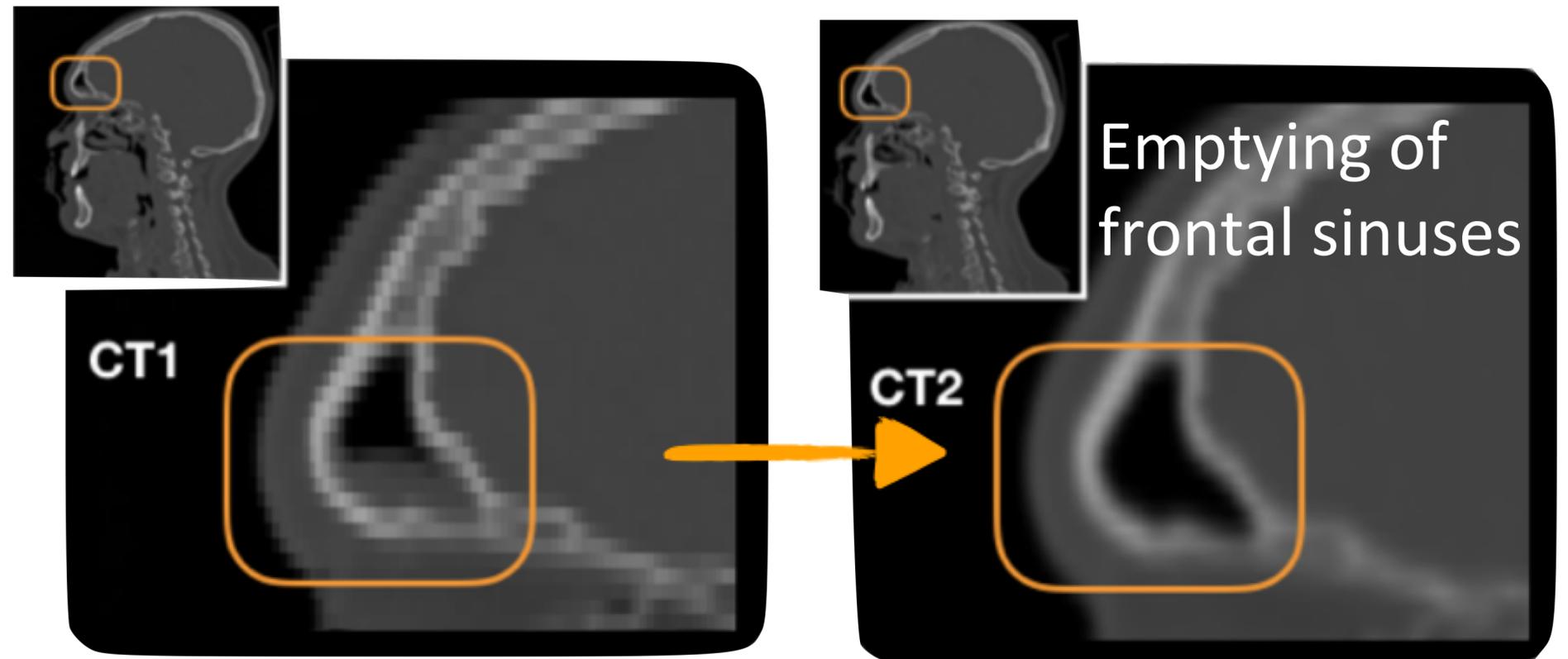
Dead time impact: beam rate fluctuations may
results in different loss between fractions



The method: workflow and monitoring strategy @ CNAO

- Carbon ion treatments at CNAO typically lasts ~ 4 weeks;
- A **CT scan** is performed and used as input for the treatment planning;
- The ^{12}C beam is delivered in ~**20 fractions**;
- The decision to perform a mid-treatment CT and eventually to re-plan the treatment is taken only accordingly to the pathology under treatment and on the basis of the collected statistics of patients with similar pathologies.

Strategy: the dis-homogeneities onset can be monitored comparing the reconstructed emission map of the fragments in different fractions of the treatment to **help the decision on when a replanning CT is needed.**



Clinical trial

A clinical trial ([ClinicalTrials.gov Identifier: NCT03662373](https://ClinicalTrials.gov/Identifier/NCT03662373)) is started at CNAO in August 2019 to evaluate the Dose Profiler capability and sensitivity in detecting morphological changes arising in pathologies of the **neck-head district**.



10 patients treated with carbon ion beam divided in **2 samples**

Pathologies where a morphological change is not expected: **check for eventual false positives**

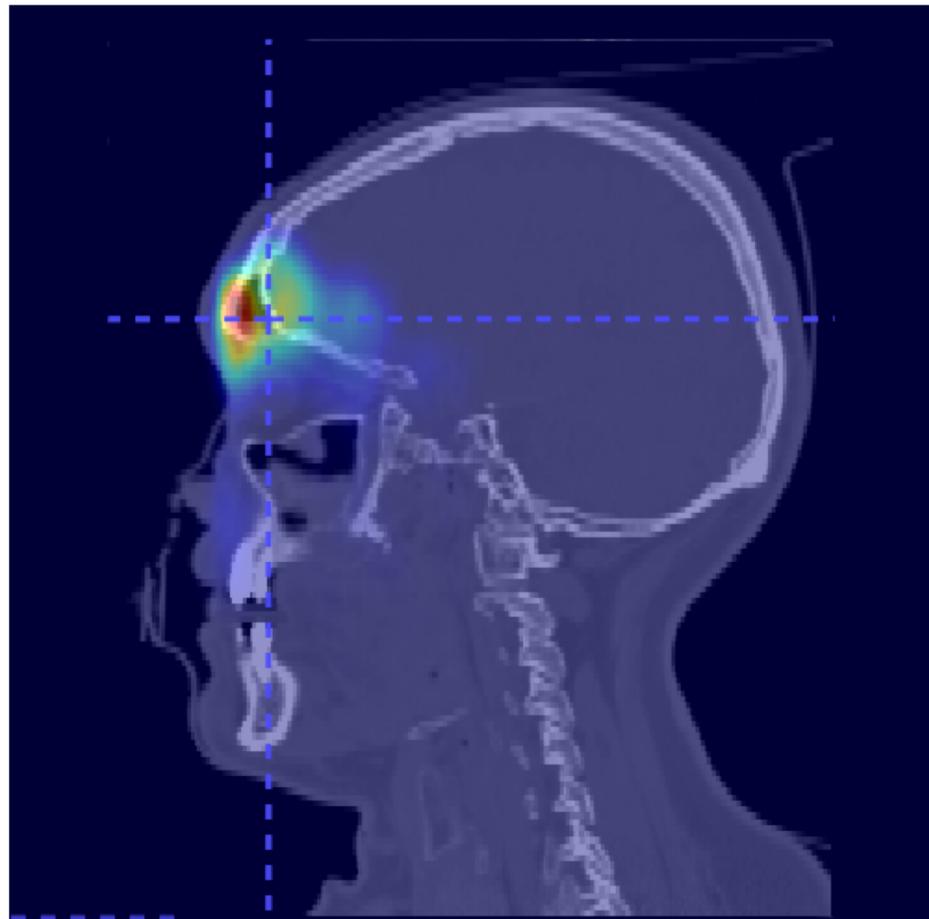
Pathologies where a morphological change is expected: **evaluate the technique feasibility and accuracy/precision**

Patient ID	Pathology	Re-evaluation CT	Re-planning
PZ1	ACC	7° fraction	no
PZ2	ACC	5° and 10° fraction	no
PZ3	ACC	no	no
PZ4	ACC	8° fraction	no
PZ5	clival chordoma	no	no
PZ6	ITAC	7° fraction	yes
PZ7	clival chordoma	no	no
PZ8	ACC	7° fraction	no
PZ9	clival chordoma	no	no
PZ10	ITAC	8° fraction	yes

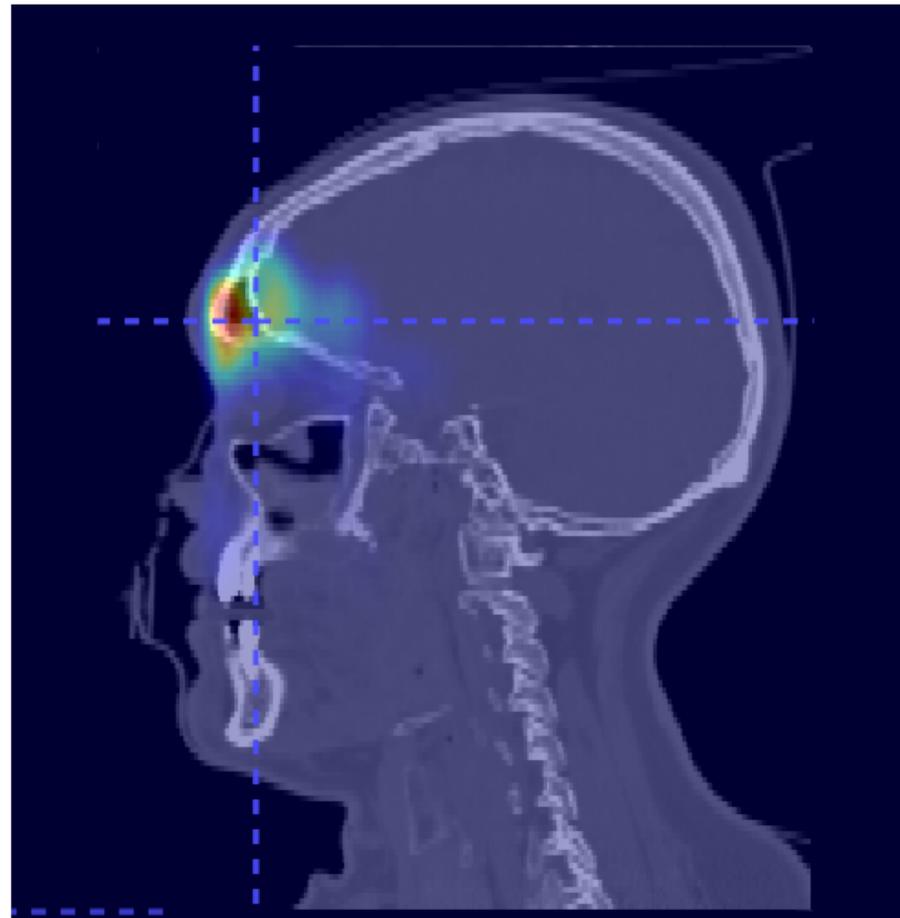


Spotting morphological variations

Fraction 1 (reference)

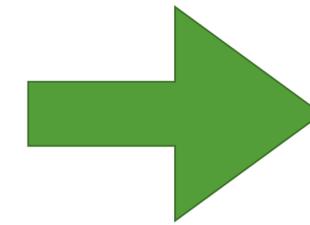


Fraction 2

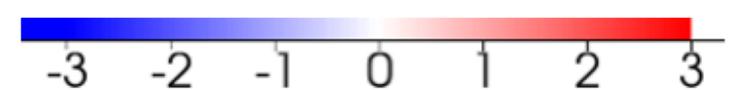
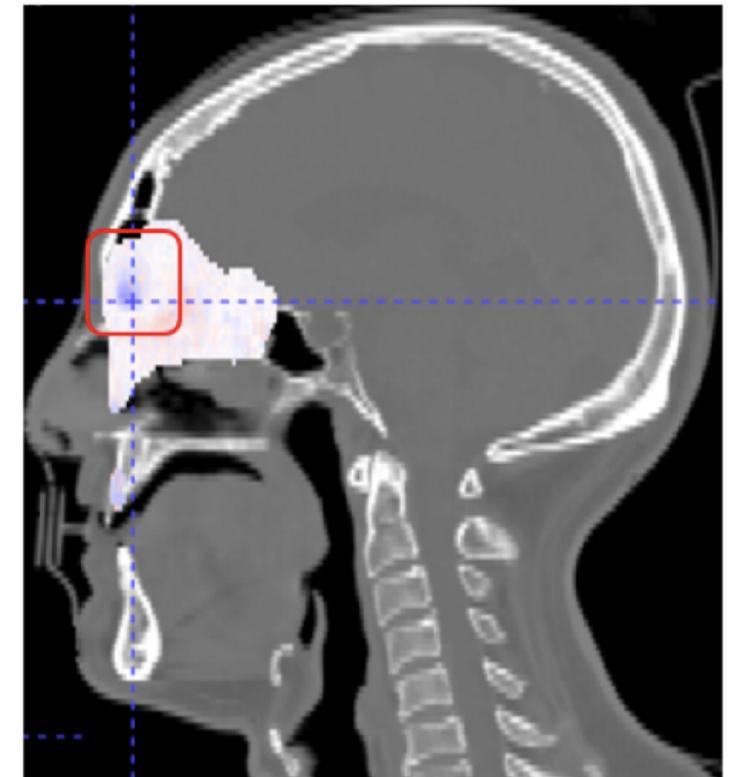


detected 3D fragment emission maps

~spatial resolution



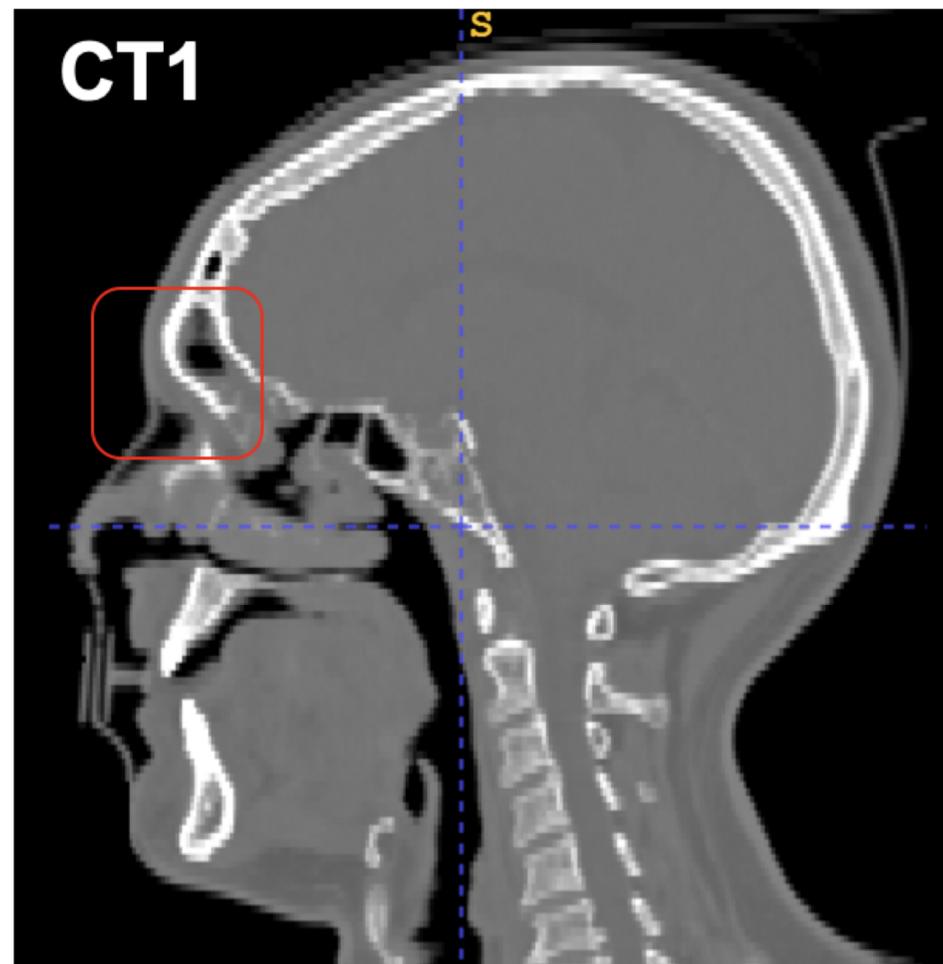
gamma-test
(7 mm/ **10%**)



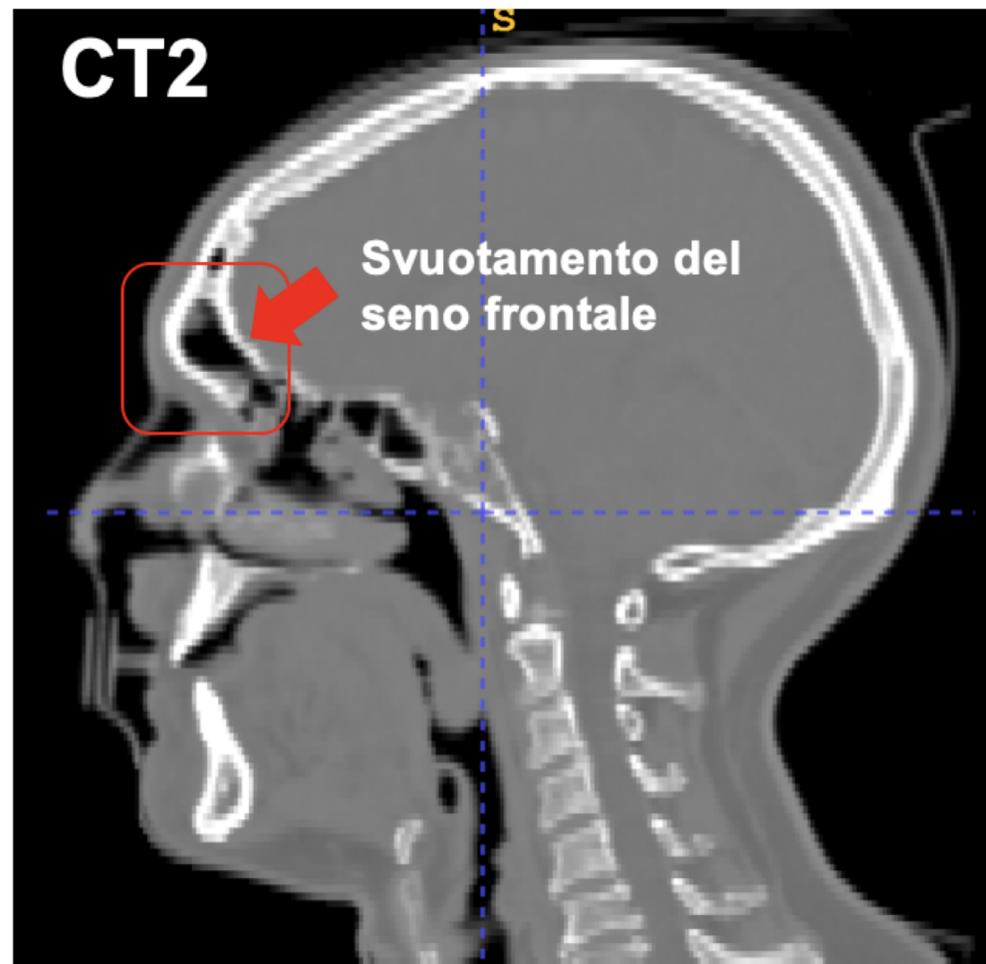
~avoid fake-positives due to stat. fluctuations

What we learned: the case of PZ4 (I)

For P4 (ACC) morphological changes has been observed in the control CT. Gamma analysis shows a clear spot located in the frontal sinuses



Planning CT

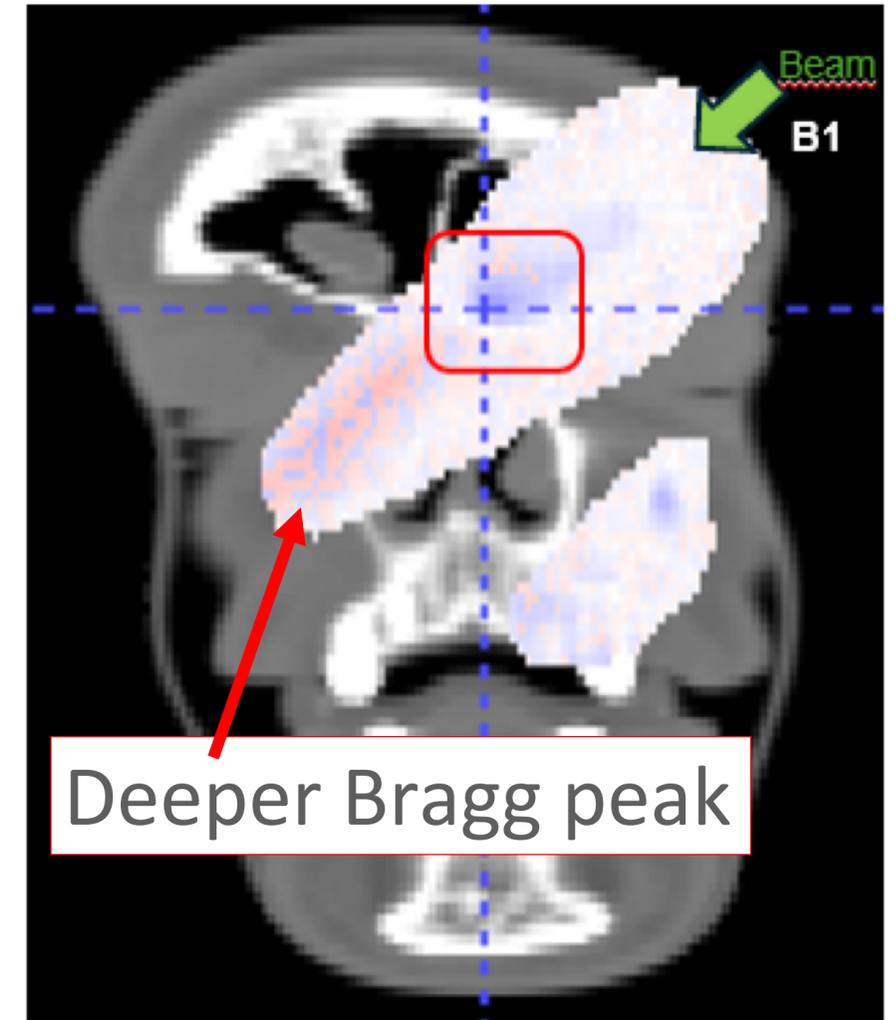
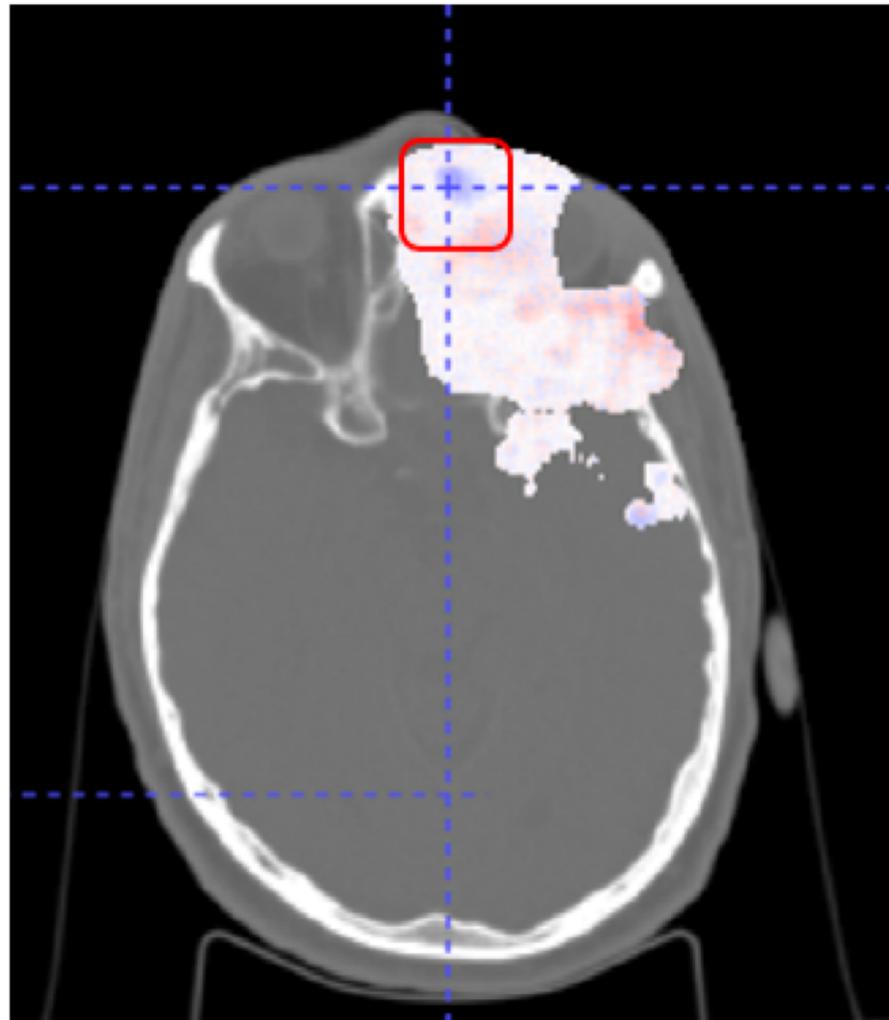


Control CT

n. Fractions	9+7
re-eval CT	After 8 fr.
Field0 (angle)	0°
Field1 (angle)	310°
Field2 (angle)	/
Dose (GyE)	68.3

What we learned: the case of PZ4 (II)

For P4 (ACC) morphological changes has been observed in the control CT. Gamma analysis shows a clear spot located in the frontal sinuses

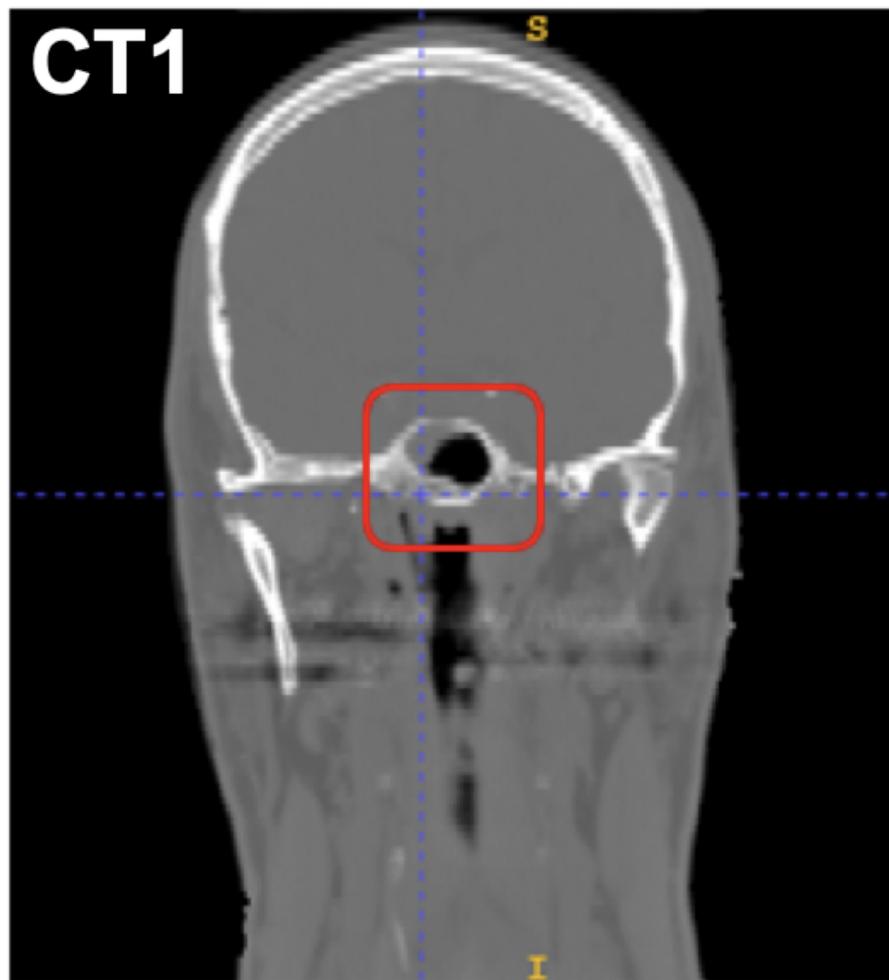


Deeper Bragg peak

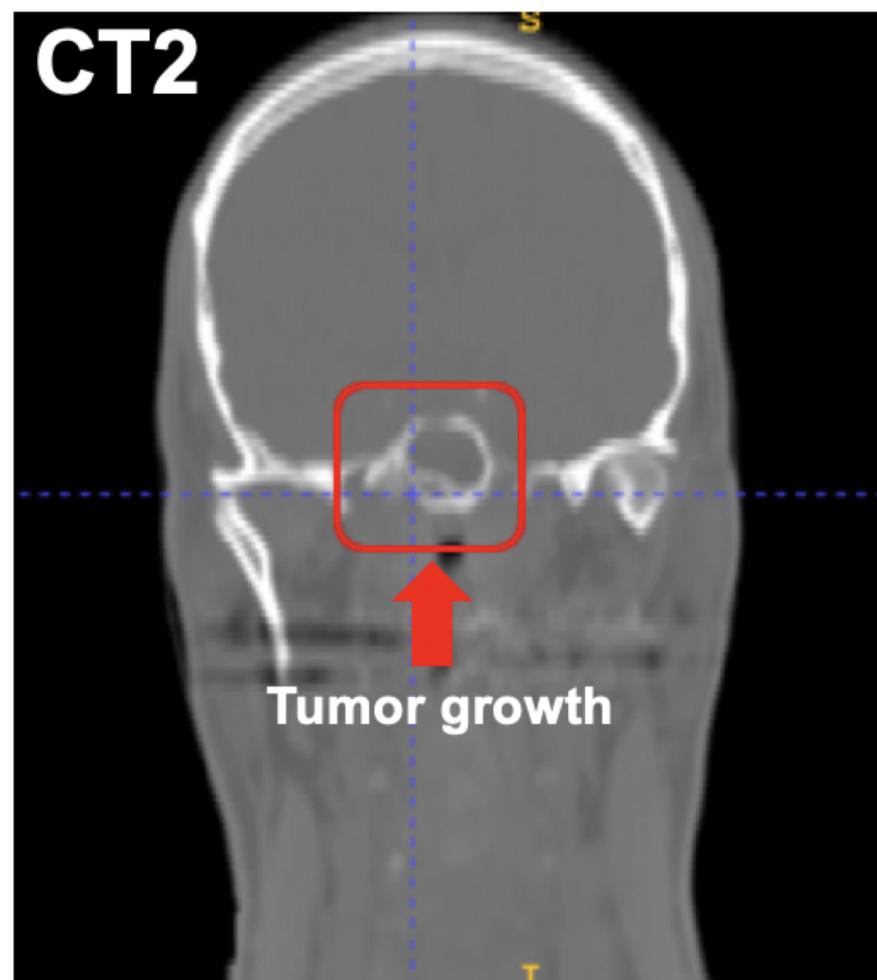
lack of secondaries
excess of secondaries

What we learned: the case of PZ6 (I)

P6 (ITAC) underwent to a serious tumor growth observed in the control CT



Planning CT



Control CT

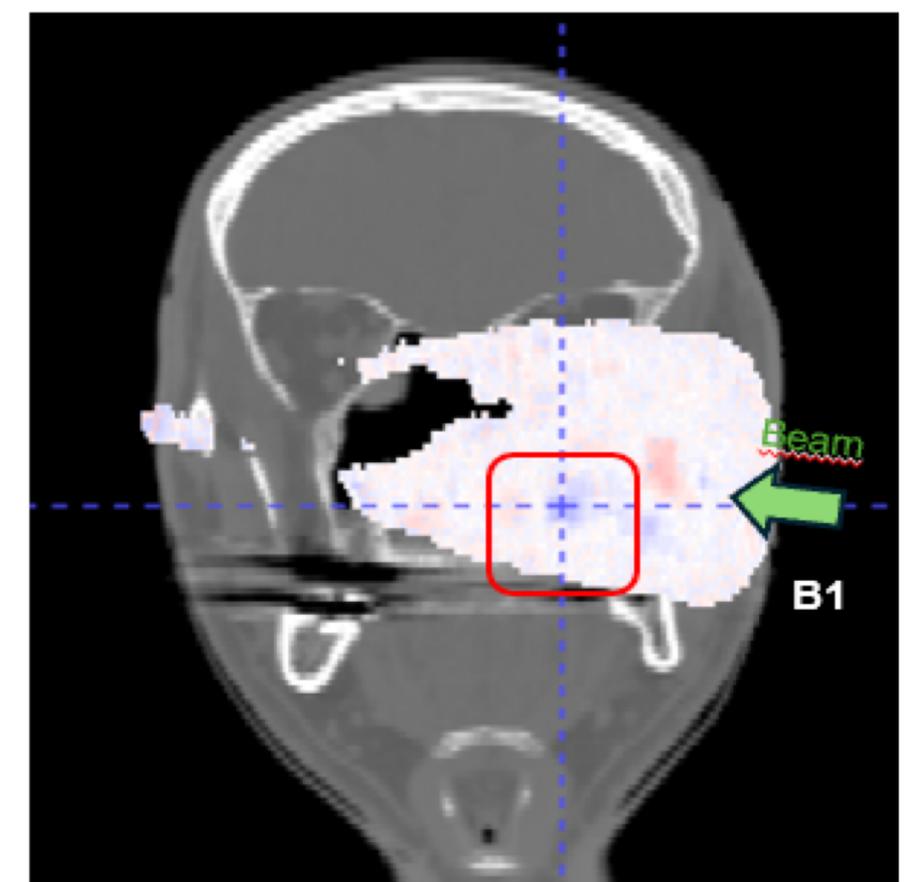
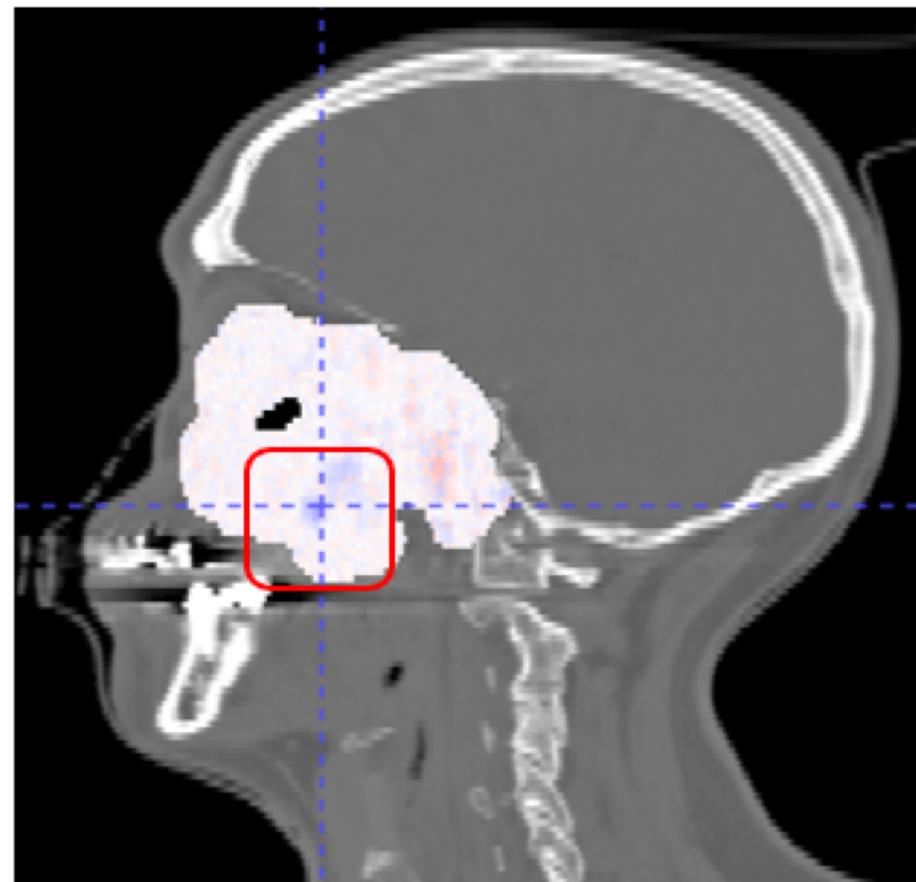
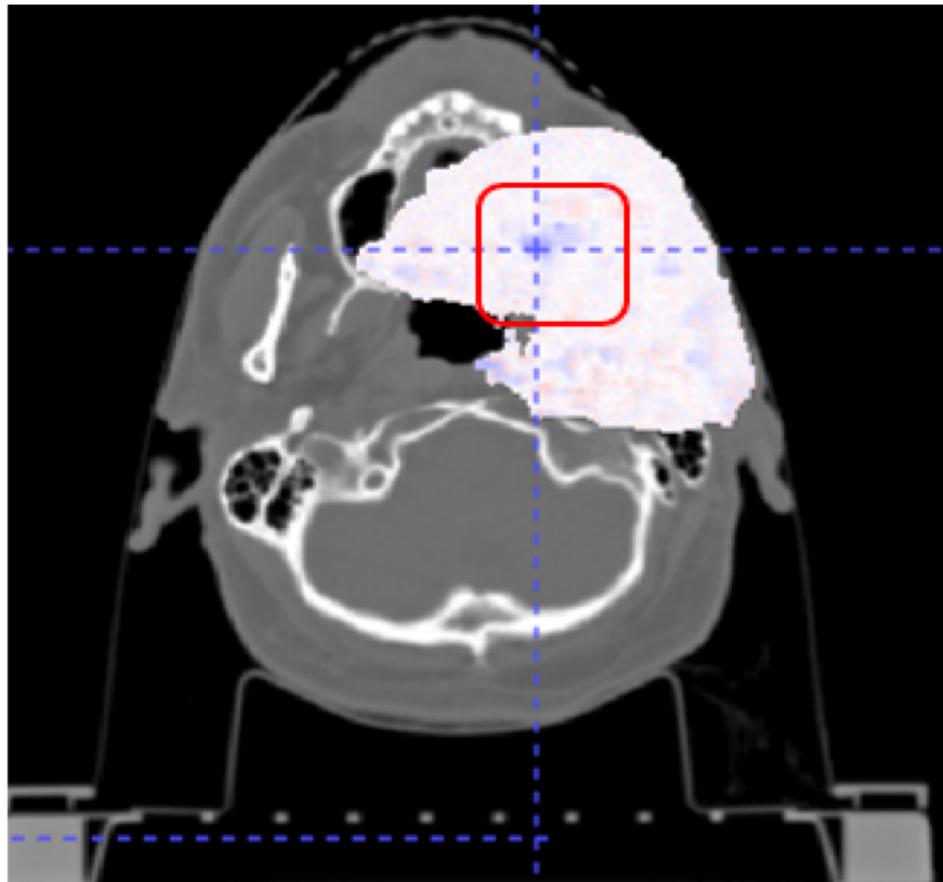
n. Fractions	9+7
re-eval CT	After 7 fr.
Field0 (angle)	0°
Field1 (angle)	180°
Field2 (angle)	270°
Dose (GyE)	65.6

What we learned: the case of PZ6 (II)

Gamma analysis did not spot the tumor growth. Possible causes:

Unfavourable FOV for fragment detection, low statistic and depth of variations

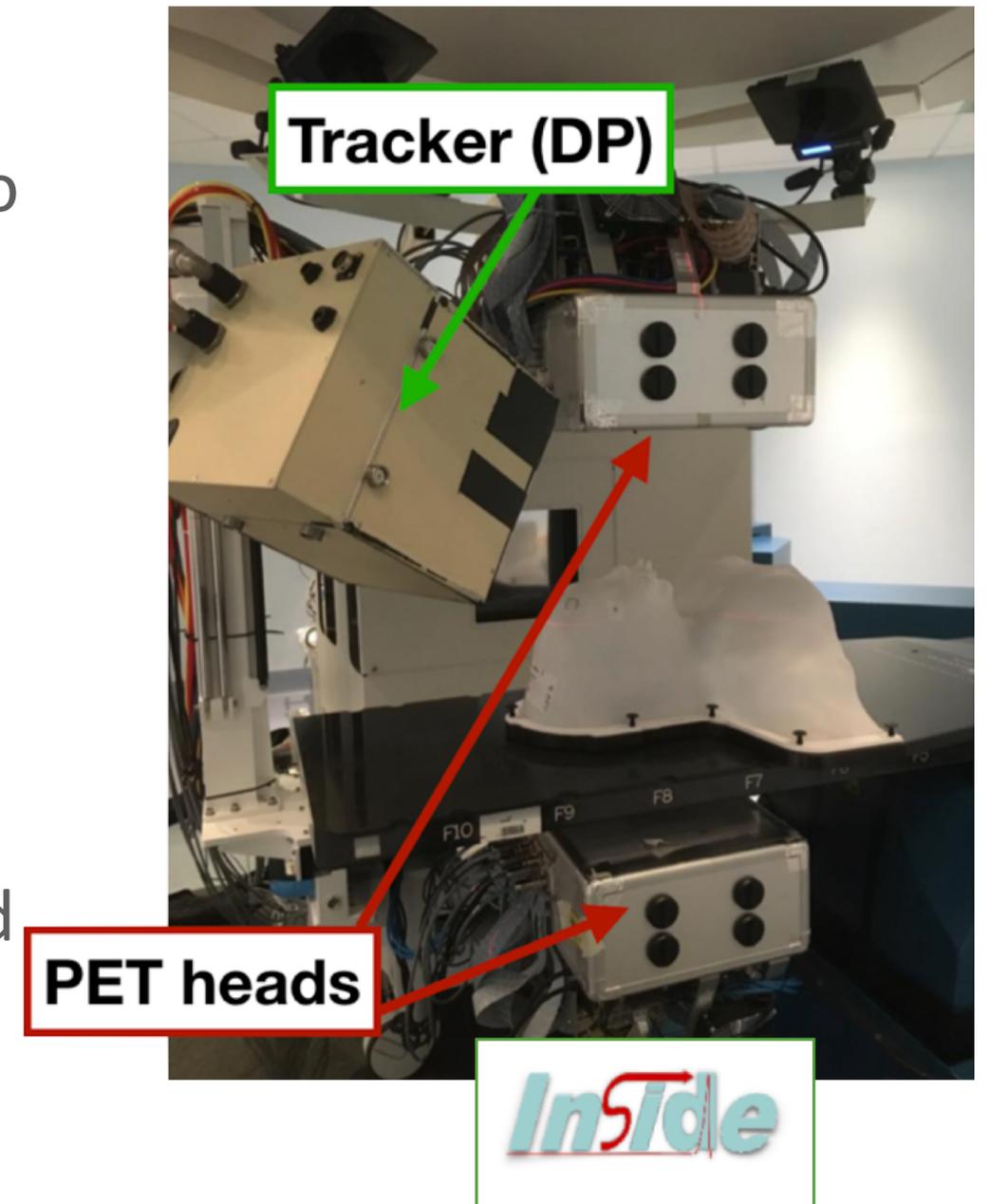
Planning CT performed ~ 20 days before the treatment start



Significant lack of secondaries, not observed on the CT

Trial restart @ CNAO: current status and perspectives

- The clinical trial has been running again for about six months. We are currently monitoring the **third patient**, and we plan to reach a total of **ten new patients treated with 12C**, in addition to the **ten already collected in 2019**
- The main objective of this new phase is to **explore the potential and the limits of the INSIDE technique**, validating the hypotheses drawn from the first cohort. In particular, we aim to verify whether the **anti-correlation with the Bragg peak**, combined with the **limited statistics**, indeed sets a hard limit on our ability to observe deep-range variations



Trial restart @ CNAO: current status and perspectives

From the first part of the trial, we have learned that it is **crucial to acquire an additional control CT during the first treatment fraction**. This is because up to **ten days may elapse** between the evaluation CT and the first treatment session, and such anatomical or setup changes can significantly affect data validation.

Thanks!

The INSIDE collaboration: Giacomo Traini, Alberto Burattini, Piergiorgio Cerello, Emanuele Maria Data, Yunsheng Dong, Veronica Ferrero, Elisa Fiorina, Gaia Franciosini, Aafke Christine Kraan, Leonardo Lampertico, Michela Marafini, Ilara Mattei, Martina Moglioni, Matteo Morrocchi, Silvia Muraro Iram Barbaro Rivas Ortiz, Vincenzo Patera, Francesco Pennazio, Flaminia Quattrini, Sahar Ranjbar, Alessandra Retico, Valeria Rosso, Alessio Sarti, Angelo Schiavi, Giancarlo Sportelli, Maria Giuseppina Bisogni