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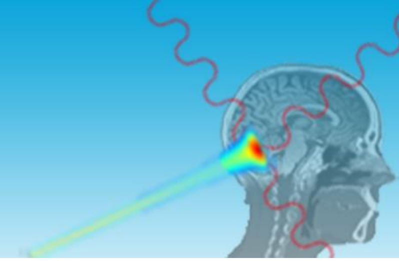

An overview on the HIGH-ART project “Hybrid imaging framework for adaptive ion beam therapy”

Gefördert durch
DFG Deutsche Forschungsgemeinschaft

Dr. Chiara Gianoli (on behalf of Prof. Katia Parodi)

7th Annual Loma Linda Workshop, August 2-4, 2021

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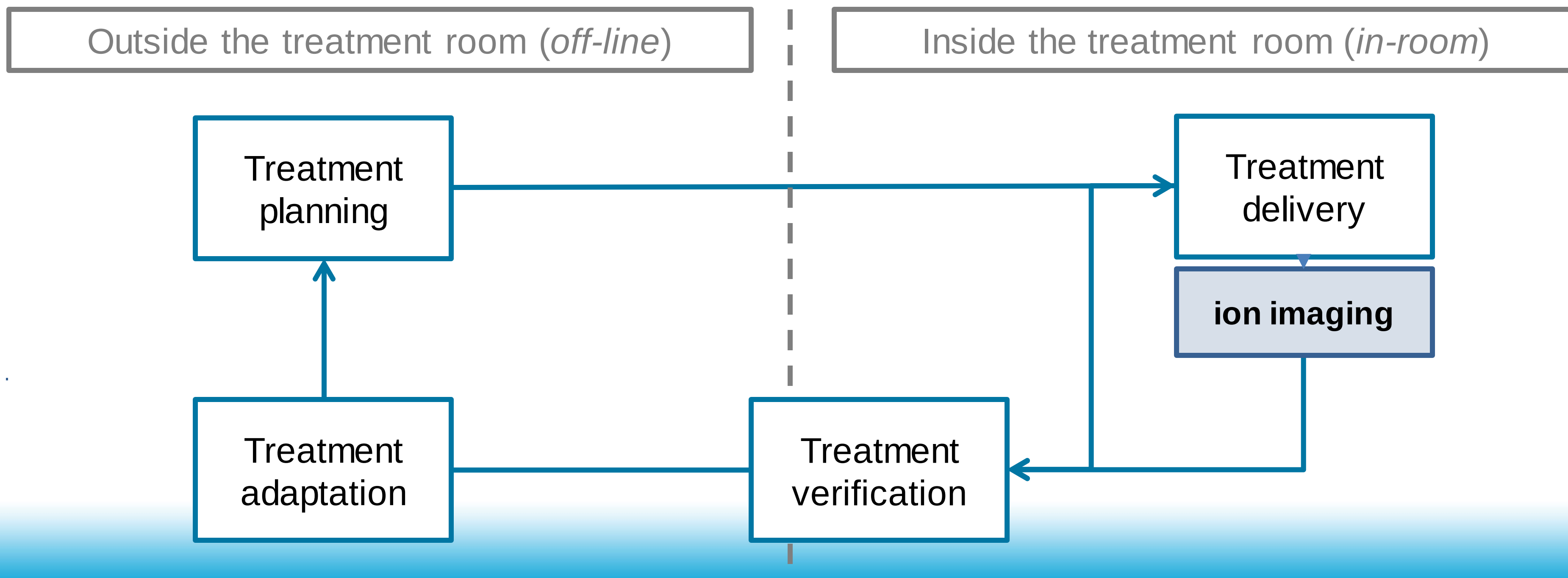
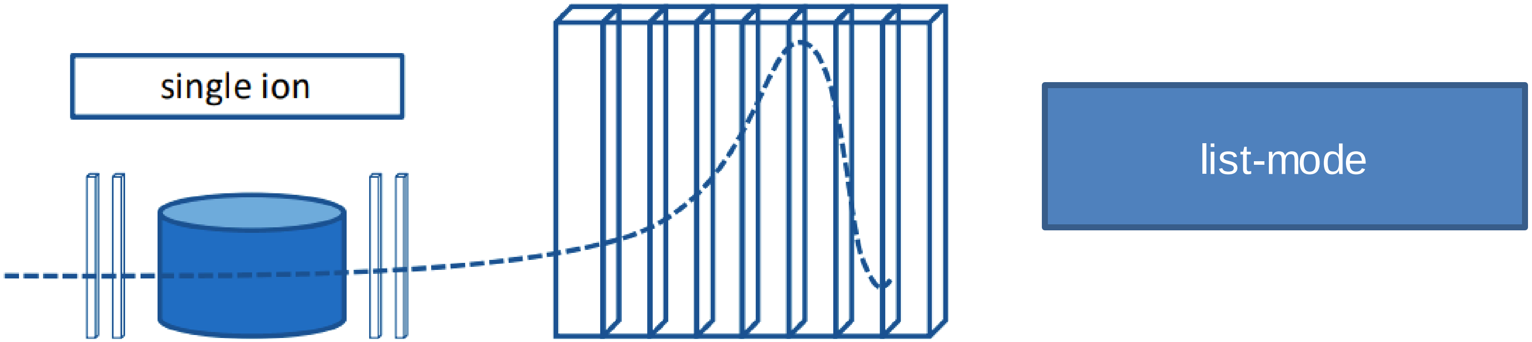
The HIGH-ART project

- Clinical workflow in ion beam therapy based on X-ray imaging but the native imaging technique for ion beam therapy is ion imaging
- Clinical translation from X-ray imaging standalone to ion imaging (standalone and in combination with X-ray imaging) is put forward to overcome the so far perceived dichotomy between X-rays and ions
- DFG project HIGH-ART approved in 2017 and just renewed in 2021 to investigate the concept of hybrid X-ray and ion imaging in adaptive ion beam therapy, inclusively consider all relevant beams (proton, helium and carbon ions) and detector technologies for future clinical deployment



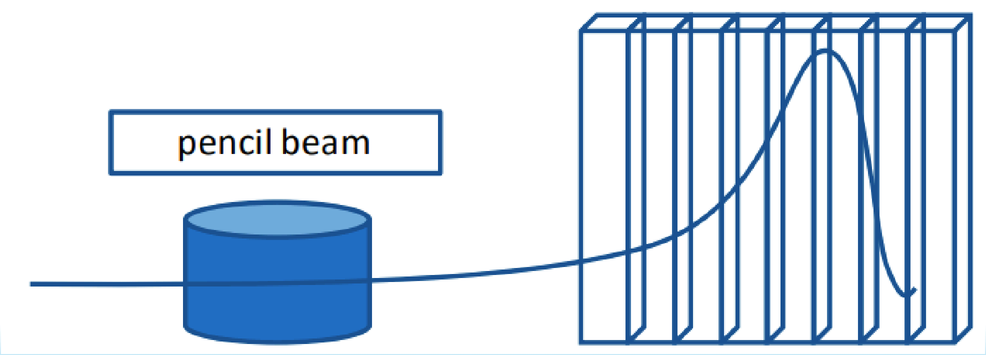
Detector configurations for ion imaging

- "Stopping power" information
  - Single absorption and detection layer measuring the residual energy of the single ion (hence, the *range*)
  - Multiple absorption layers interleaved by detection layers measuring the energy loss of the single ion (hence, the *range*)
    - The *range* is then converted to water equivalent thickness (WET)
- "Scattering power" information
  - Single or double thin detection layers (trackers) measuring *position* and *angle* of the single ion prior and after the object of interest



Detector configurations for ion imaging

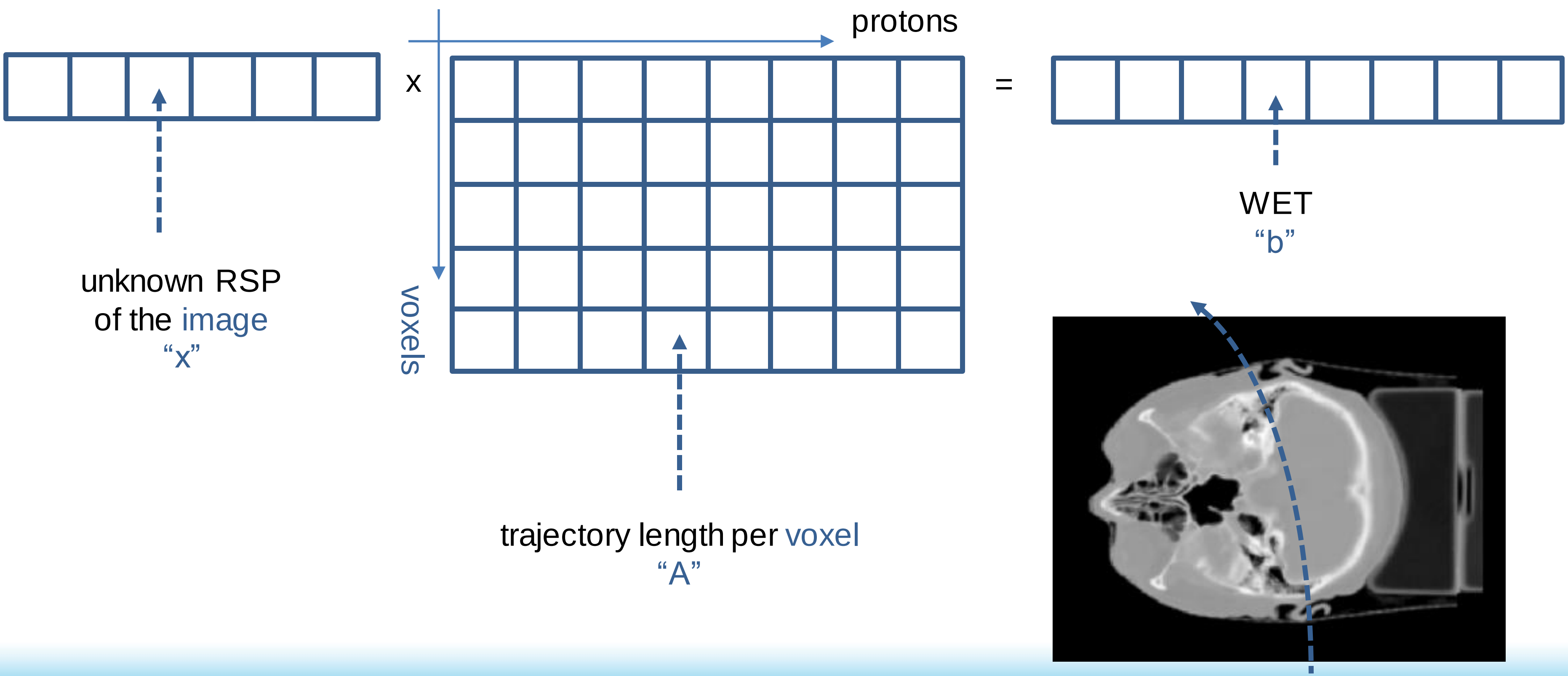
- "Stopping power" information
  - Single absorption and detection layer measuring the residual energy of the pencil beam (hence, the *mean range*)
    - The *mean range* is converted to WET
  - Multiple absorption layers interleaved by detection layers measuring the energy loss of the pencil beam (hence, the *mixed range*) at a single initial energy
  - Single thin absorption and detection layer measuring the energy loss at multiple initial energies of the pencil beam (hence, the *mixed range*) (Ref. presentation of *Katrin Schnürle*)
    - The *mixed range* is firstly resolved and then converted to a WET histogram (the *mode* WET component or the *mean* WET component are selected)



integration-mode

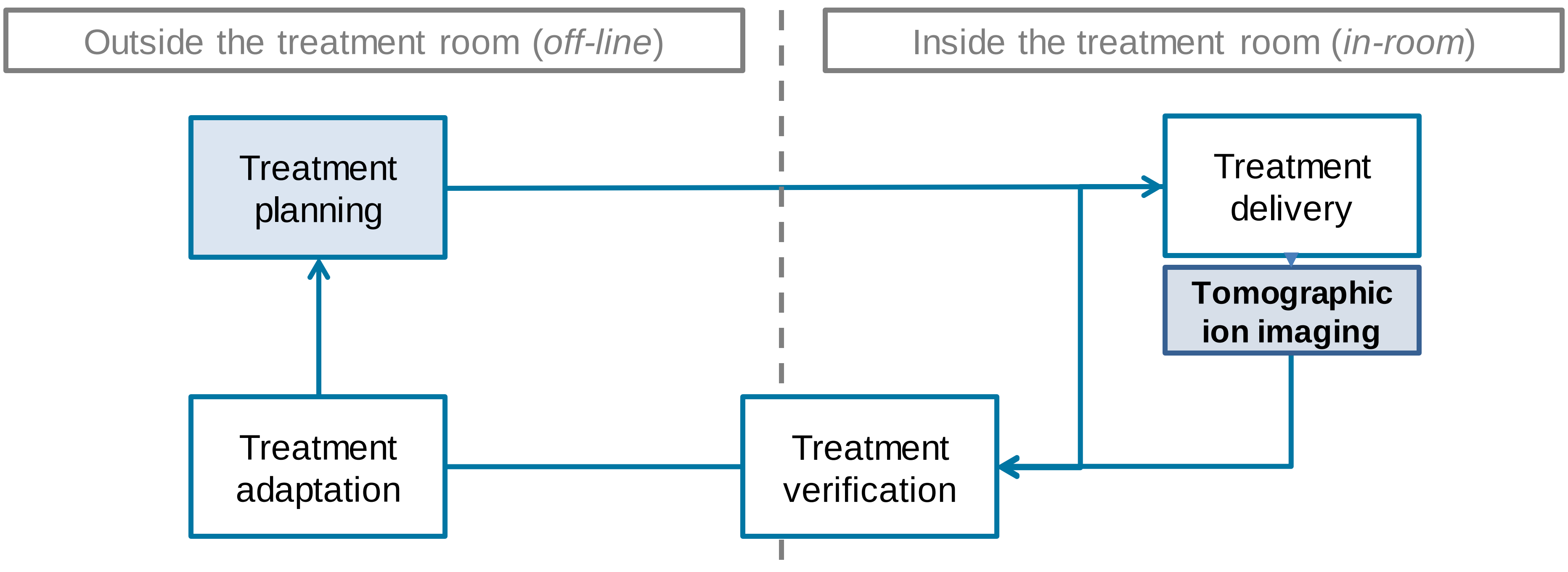
Ion CT

- The ion radiography collects the WET, modeled as integral RSP along the ion (list-mode) or pencil beam (integration-mode) trajectory according to the so called forward-projection model
    - Based on the forward-projection model, an ion tomography expressed in RSP can be reconstructed from several ion radiographies



The role of ion imaging in ion beam therapy

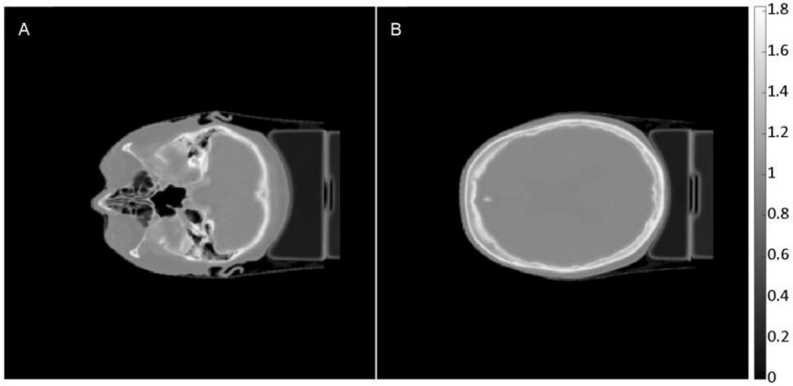
- The calibration inaccuracies of the X-ray CT, due to semi-empirical calibration of Hounsfield Unit (HU) into Relative Stopping Power (RSP), can be minimized by the ion tomography
  - The ion tomography replaces the X-ray CT in treatment planning



Simulations

- Monte Carlo simulations of protons, helium and carbon ions radiographies in pencil beam scanning for ideal list-mode detector configuration based on a customized FLUKA Monte Carlo platform (~1.9 mGy for 180 radiographies spaced by 1°)

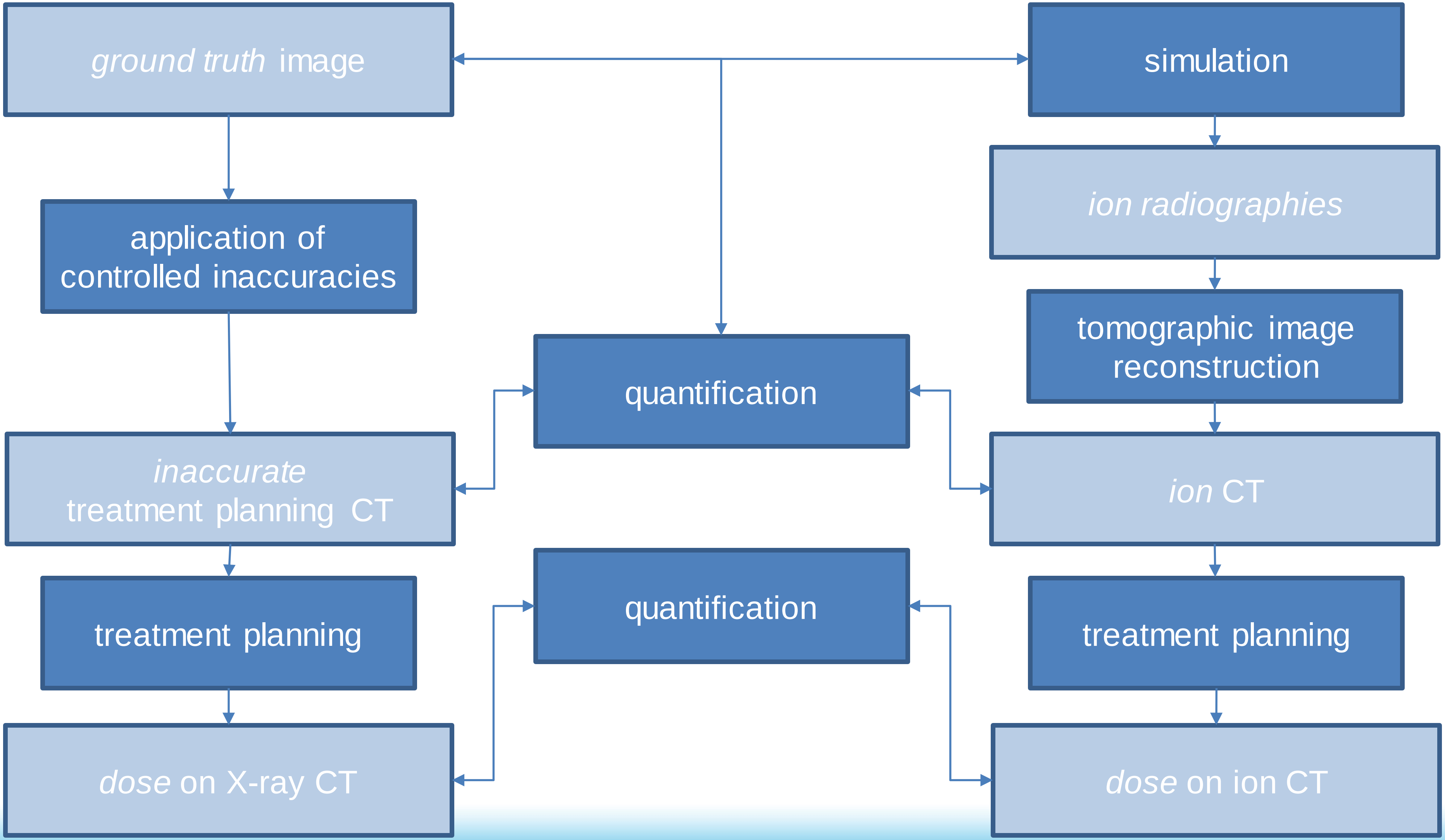
	Protons	*Helium ions*	*Carbon ions*
Energy of the pencil beam	199.44 MeV	199.03 MeV/u	385.18 MeV/u
Ions per pencil beams	400	100	20
Standard deviation of the beam spot size	8.5 mm	5.1 mm	3.5 mm



- Trajectory estimation for tomographic image reconstruction based on:
    - The most likely path based on the *positions* and *angles* of the single ion provided with the scattering model of the ion in water (*Schneider and Pedroni 1994*, *Schulte et al 2008*)
    - The "phenomenological" cubic spline approximation of the most likely path (*Li et al 2006*, *Collins-Fekete et al 2015*)
    - Linear interpolation based on the *positions* of the single ion (straight trajectory)

Meyer, S., Kamp, F., Tessonnier, T., Mairani, A., Belka, C., Carlson, D. J., Gianoli, C., & Parodi, K. (2019). Dosimetric accuracy and radiobiological implications of ion computed tomography for proton therapy treatment planning. *Physics in medicine and biology*, 64(12), 125008

Methodological workflow

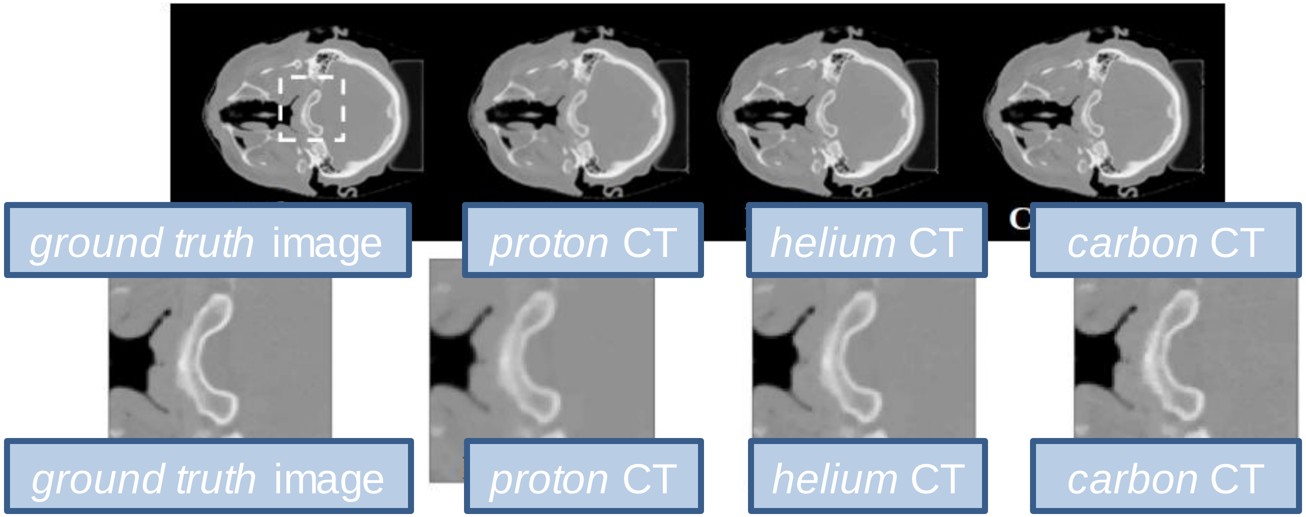


Results

- Superiority of curved ion trajectories (most likely path and its approximation) compared to straight trajectories, especially for protons

- Superior image quality for tomographic image reconstruction based on ordered subset simultaneous algebraic reconstruction technique coupled with total variation superiorization (*Penfold et al 2010*)

- Superior dose calculation accuracy, lower physical and potentially biological dose exposure for ion imaging, compared to X-ray imaging



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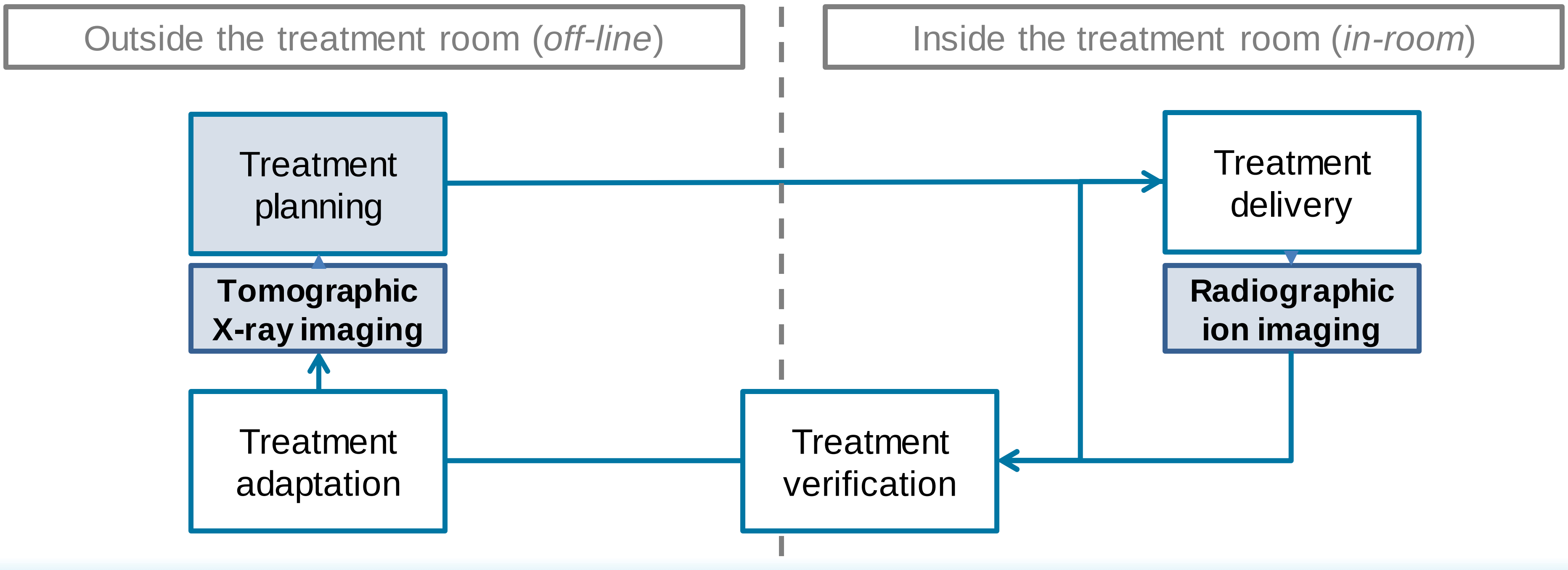
Meyer, S., Pinto, M., Parodi, K., & Gianoli, C. (2021). The impact of path estimates in iterative ion CT reconstructions for clinical-like cases. *Physics in Medicine & Biology*. (in press)

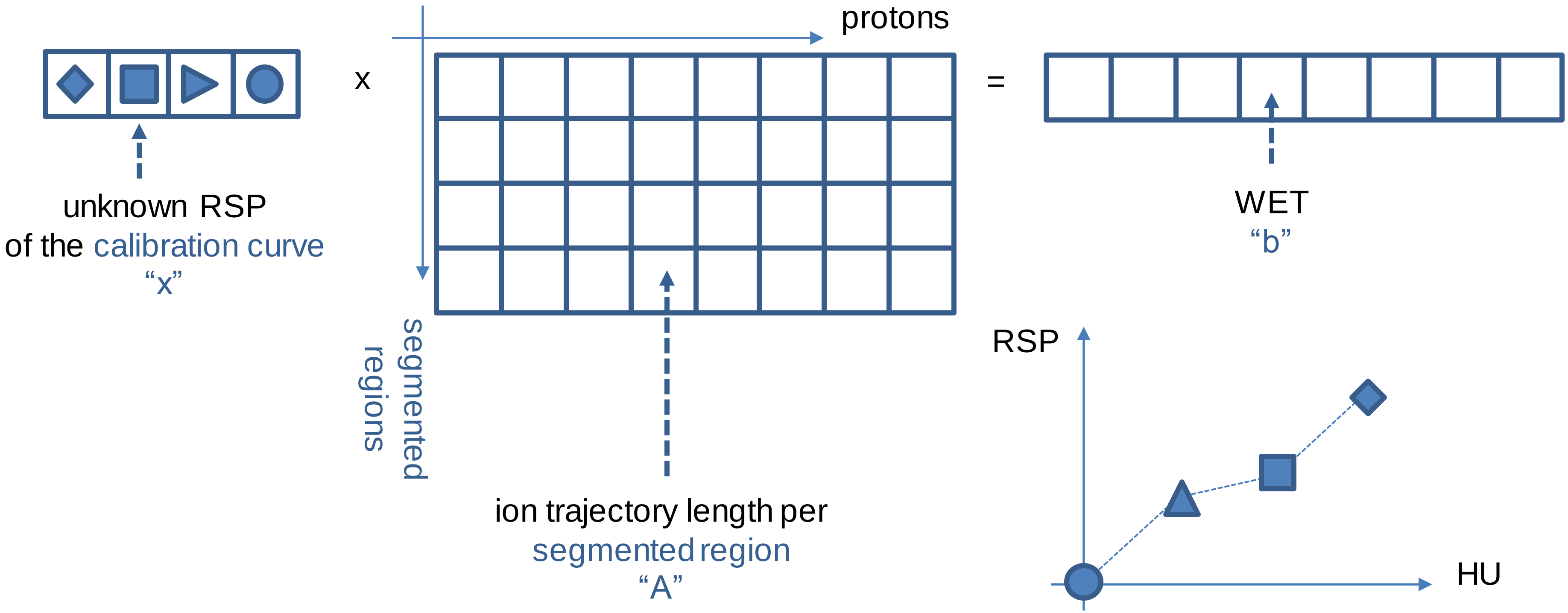
The role of ion imaging in ion beam therapy

- The calibration inaccuracies of the X-ray CT can be minimized relying on ion radiographies
  - Anatomical registration between X-ray CT and ion radiographies is required
  - The anatomical inaccuracies of the X-ray CT can be minimized relying on ion radiographies (Ref. presentation of Dr. *Prasannakumar Palaniappan*)

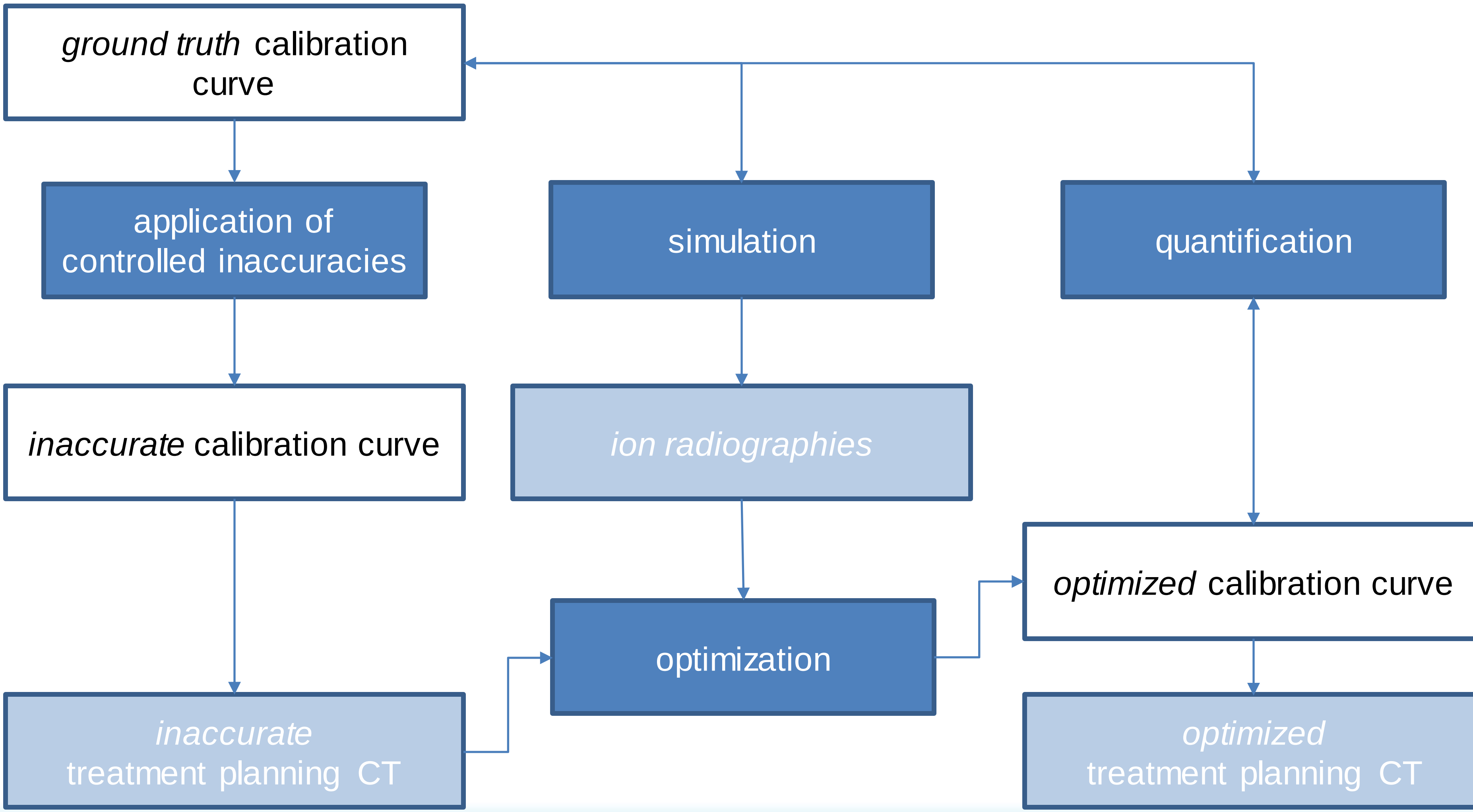


Ion radiographies and X-ray CT

- The ion radiography collects the WET, modeled as integral RSP along the ion (list-mode) or pencil beam (integration-mode) trajectory according to the so called forward-projection model
  - The same forward-projection model can be expressed in function of the calibration curve to optimize the inaccurate calibration of the X-ray CT

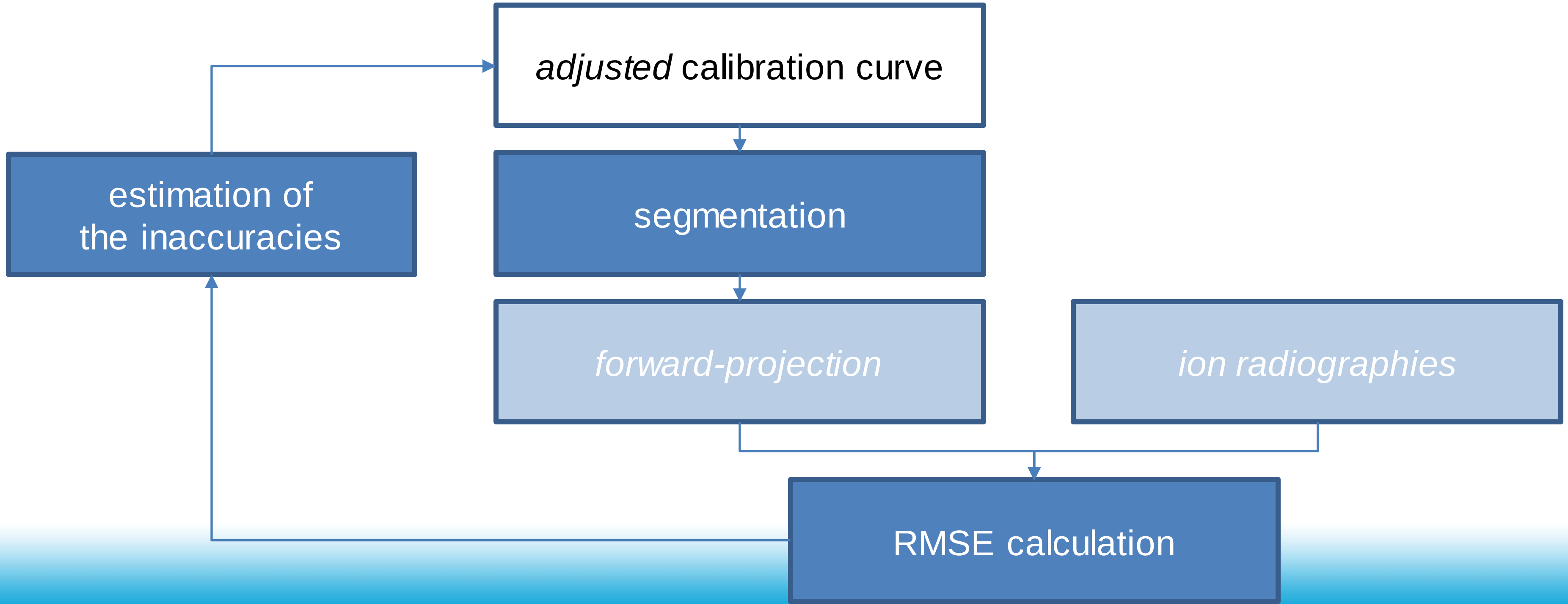


Methodological workflow



Workflow of the optimization algorithm

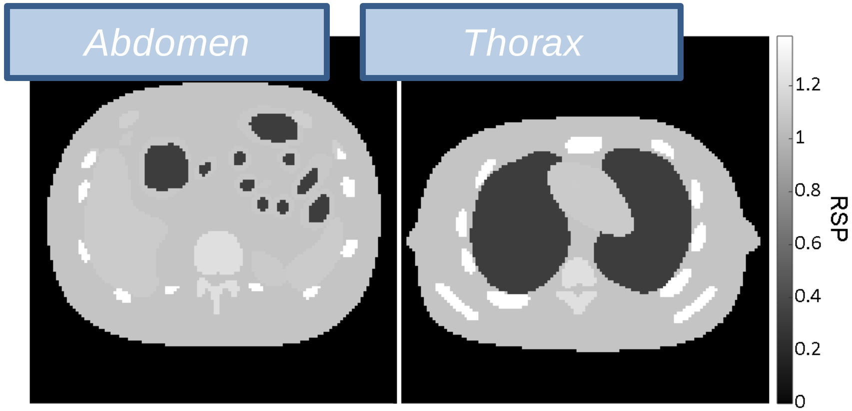
- The optimization can be implemented as:
  - Linear (*Schneider et al 2005*, *Collins-Fekete et al 2017*, *Zhang et al 2018*, *Krah et al 2019*) if the ion trajectory length in A accounts for the RSP of the inaccurate X-ray CT so that x is just the "RSP correction vector"
  - Non-linear (*Doolan et al 2015*, *Gianoli et al 2020*) if the ion trajectory length in A accounts for the RSP of the iteratively optimized X-ray CT so that x is the "RSP vector"



Simulations

- Analytical simulations of proton radiographies in pencil beam scanning for list-mode and integration-mode detector configurations
  - Trajectory simulation based on most likely path provided with the scattering model of the ion extended to non-uniform water equivalent materials
  - Trajectory estimation based on most likely path provided with the scattering model of the ion in uniform water (conventional trajectory estimation)

Energy of the pencil beam	280 MeV
Protons per pencil beams	100, 75, 50, 25, 10, 5
Standard deviation of the beam spot size	0.0 cm, 0.3 cm

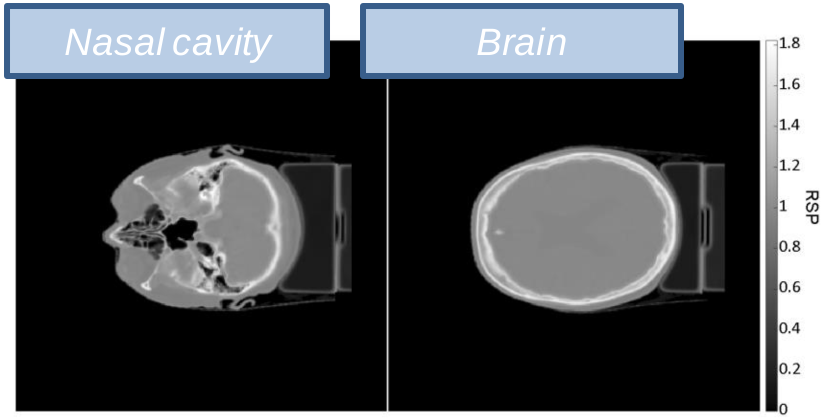


Gianoli, C., Meyer, S., Magallanes, L., Paganelli, C., Baroni, G., & Parodi, K. (2019). Analytical simulator of proton radiography and tomography for different detector configurations. *Physica Medica*, 59, 92-99

Simulations

- Monte Carlo simulations of protons, helium and carbon ions radiographies in pencil beam scanning for ideal list-mode and ideal integration-mode detector configurations
    - Trajectory simulation based on a customized FLUKA Monte Carlo platform
    - Trajectory estimation based on most likely path provided with the scattering model of the ion in uniform water (conventional trajectory estimation)

	Protons	*Helium ions*	*Carbon ions*
Energy of the pencil beam	199.44 MeV	199.03 MeV/u	385.18 MeV/u
Ions per pencil beams	400, 10000	100, 2500	20, 500
Standard deviation of the beam spot size	8.5 mm	5.1 mm	3.5 mm



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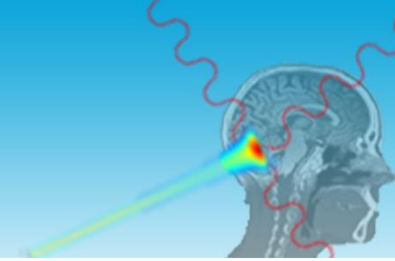


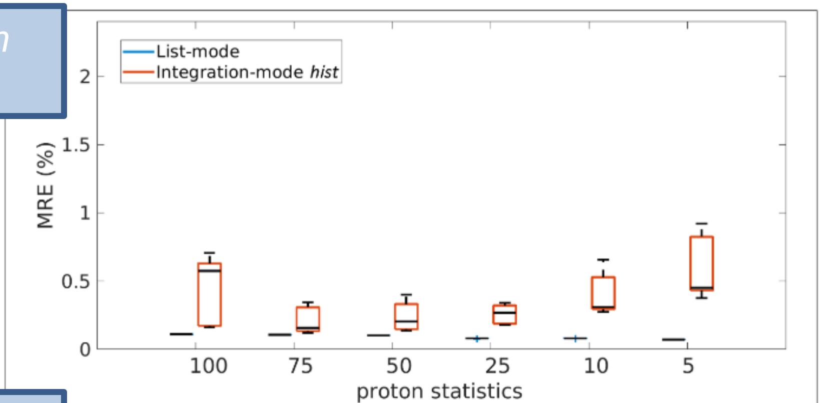
Results

- Integration-mode detector configuration when the *mode* WET component or the *mean* WET component are used is not successful in minimizing the calibration inaccuracies

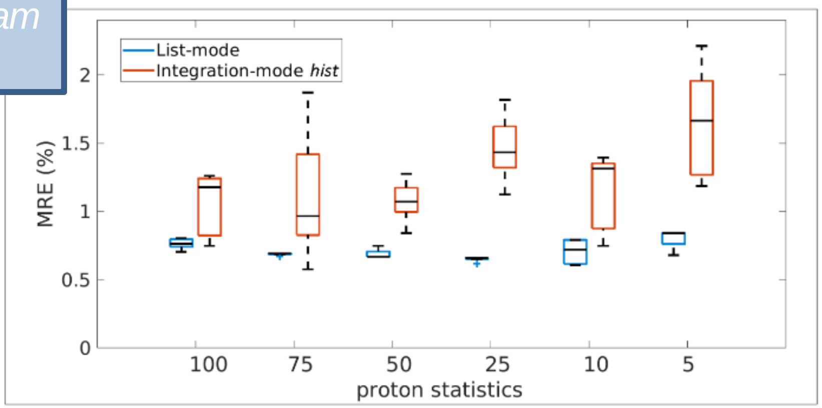
- Successful results are obtained when the entire WET histogram is used

- The beam spot size introduces intrinsic inconsistencies in the forward-projection model (between the proton radiography and the forward-projection of the ground truth image) that compromise the results

Ideal beam spot size



Realistic beam spot size

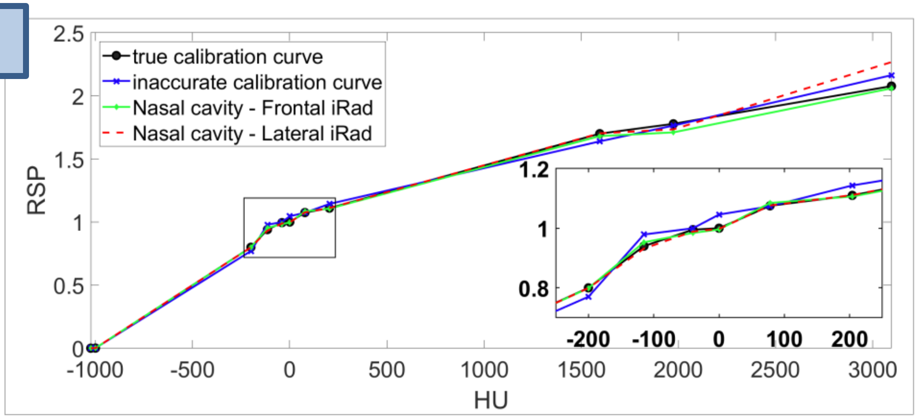


Gianoli, C., Göppel, M., Meyer, S., Palaniappan, P., Rädler, M., Kamp, F., ... & Parodi, K. (2020). Patient-specific CT calibration based on ion radiography for different detector configurations in 1H, 4He and 12C ion pencil beam scanning. Physics in Medicine & Biology, 65(24), 245014.

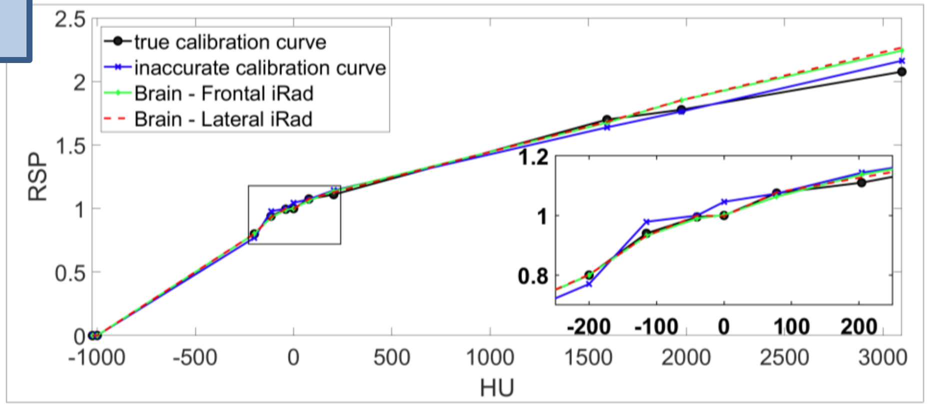
Results

- The forward-projection model for list-mode detector configuration is accurate enough to potentially minimize the calibration inaccuracies

Nasal cavity



Brain



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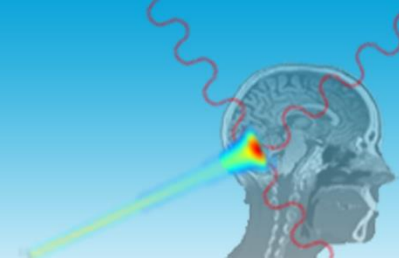
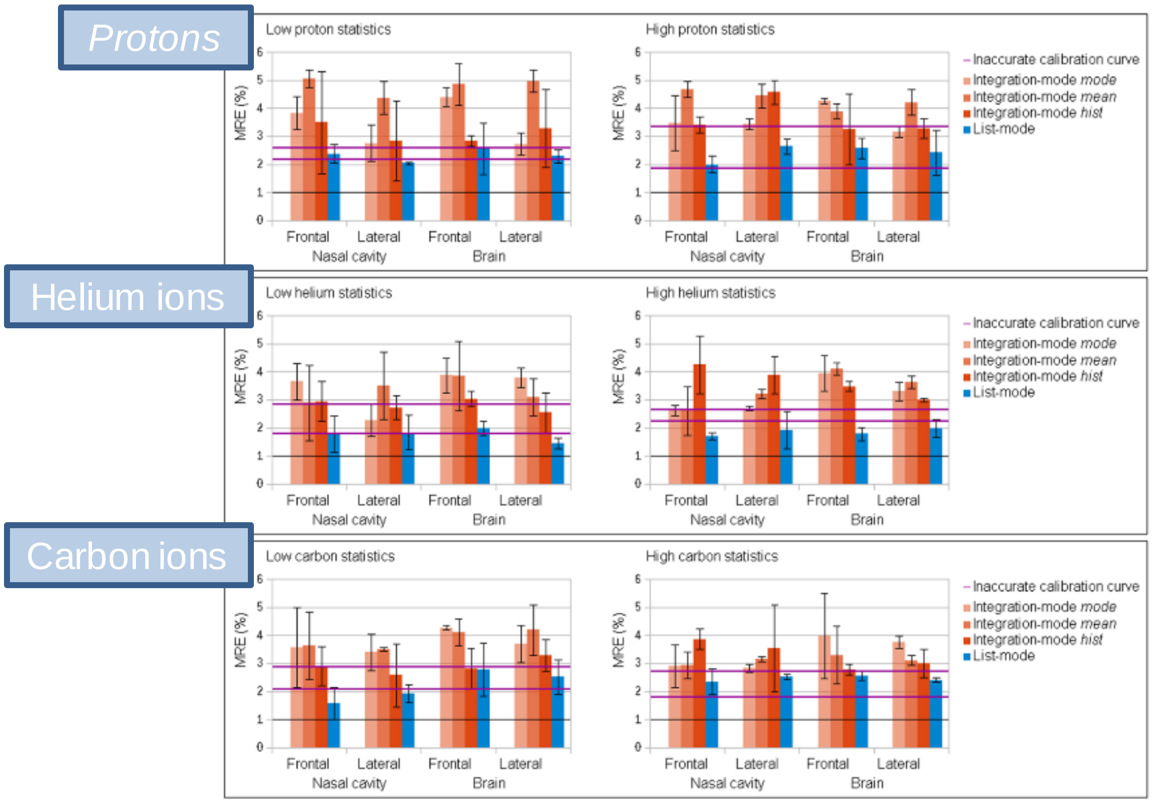


Results

- The forward-projection model for integration-mode detector configuration is affected by intrinsic inconsistencies in the same order of magnitude as the calibration inaccuracies



- The forward-projection model is based on straight trajectories, thus being valid only for ions that do not deviate from the pencil beam trajectories
  - Protons are penalized by larger scattering and beam spot size
  - Helium ions benefit from the compromise between deviations (scattering and beam spot size) and statistics
  - Carbon ions are penalized by the statistics

Gianoli, C., Göppel, M., Meyer, S., Palaniappan, P., Rädler, M., Kamp, F., ... & Parodi, K. (2020). Patient-specific CT calibration based on ion radiography for different detector configurations in 1H, 4He and 12C ion pencil beam scanning. Physics in Medicine & Biology, 65(24), 245014.

Current/future works

- List-mode detectors represents the optimal configuration

- Integration-mode detectors are identified as promising configuration for clinical translation but dedicated imaging methodologies are required to approach the state-of-the-art as for list-mode detector configuration ("making the most of the available information")

  - The forward-projection model for integration-mode detector configuration is valid for a continuous WET histogram per each pencil beam, which is challenging within clinically acceptable dose exposure

  - To overcome the intrinsic inconsistencies of the forward-projection model, different solutions are proposed:

    - More accurate model based on the entire WET histogram, extendable to tomographic image reconstruction

C. Seller Oria, S. Meyer, E. De Bernardi, K. Parodi and C. Gianoli. A Dedicated Tomographic Image Reconstruction Algorithm for Integration-Mode Detector Configuration in Ion Imaging. In Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), 2018 IEEE.

  - More accurate model based on combined information from X-ray imaging (treatment planning X-ray CT or in-room X-ray imaging)

  - Data-driven model based on Monte Carlo simulations (provided with the ground truth image/calibration curve)

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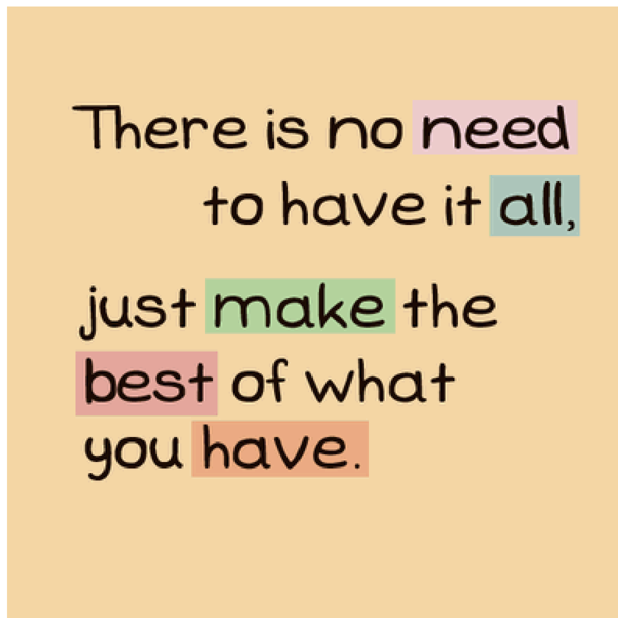

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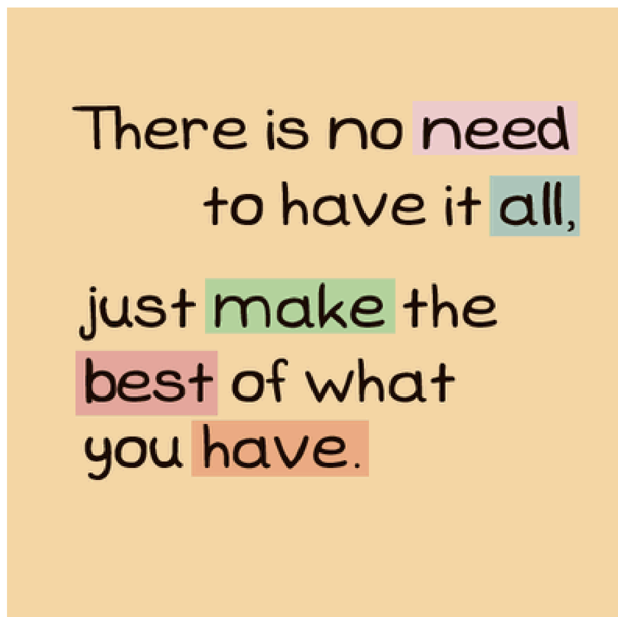
Thanks for your attention!



Additional slides

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	Detector	Object of interest	Optimization	Quantification
Schneider et al (2005)	List-mode (straight protons, averaged)	Real dog patient	Linear (random searching)	No ground truth, quantification with respect to WETs
Doolan et al (2015)	Integration-mode	Real tissue samples	Non-linear (Nelder-Mead algorithm)	No ground truth, quantification with respect to WETs
Collins-Fekete et al (2017)	List-mode	Monte Carlo simulations of anthropomorphic phantom	Linear	Ground truth (the true RSPs), quantification with respect to a “clinical curve”
Zhang et al (2018)	Integration-mode	Physical phantom	Linear, regularized	Ground truth (the true RSPs)
Krah et al (2019)	Integration-mode	Monte Carlo simulations of anthropomorphic phantom	Linear, regularized	Ground truth (the true RSPs) but regularization based on the ground truth…