Proton radiography applications in an adaptive proton therapy workflow

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KWF KANKER BESTRIJDING

INCONTROL
Clinical Control Infrastructure for Proton Therapy Treatments

Introduction

Koehler AM. **„Proton radiography“**. Science. 1968 Apr 19;160(3825):303-4. doi: 10.1126/science.160.3825.303. PMID: 17788234

*‘Energetic protons from an accelerator **may be used** to produce radiographs showing unusually high contrast but relatively poor spatial resolution’.*

Johnson RP. **“Review of medical radiography and tomography with proton beams”**. Rep Prog Phys. 2018 Jan;81(1):016701. doi: 10.1088/1361-6633/aa8b1d. PMID: 28884707.

*‘The recent global expansion of hadron therapy, coupled with modern advances in computation and particle detection, has led several collaborations around the world to develop **prototype** detector systems and associated reconstruction codes for proton computed tomography (pCT), as well as more simple proton radiography, with the ultimate intent to use such systems in clinical treatment planning and verification.’*

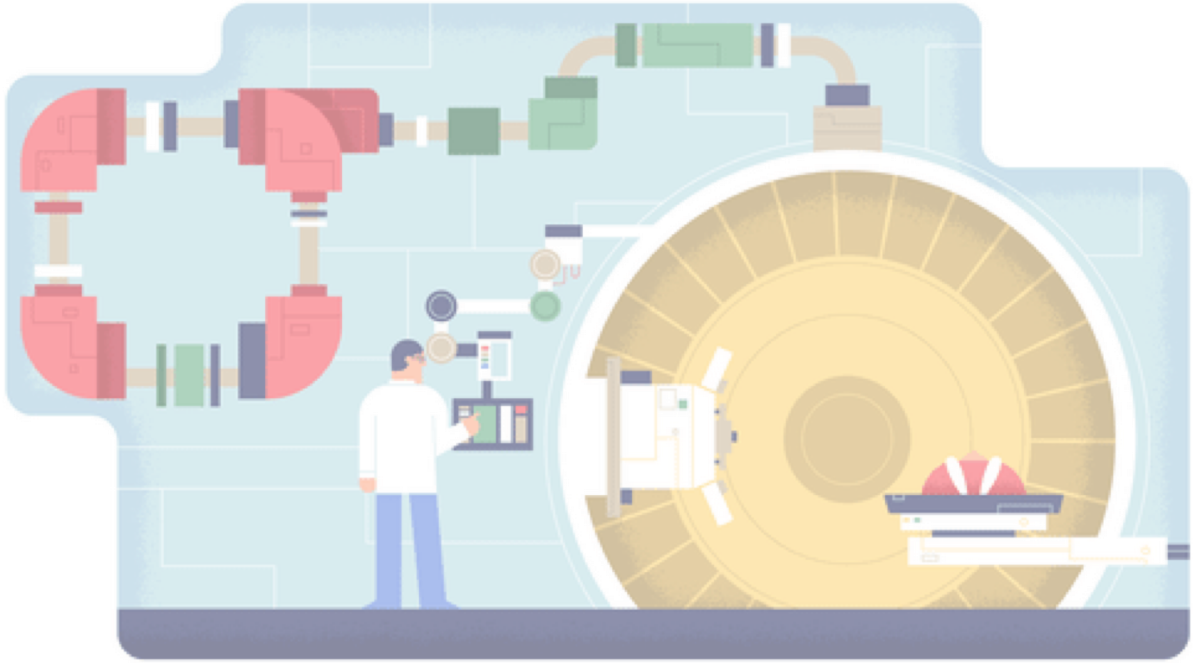
For proton radiography, how close have we come to clinical implementation and use in the context of adaptive proton therapy?

Introduction – Adaptive Proton Therapy

Reference / planning 3D imaging and contouring

Nominal plan generation

Quality assurance

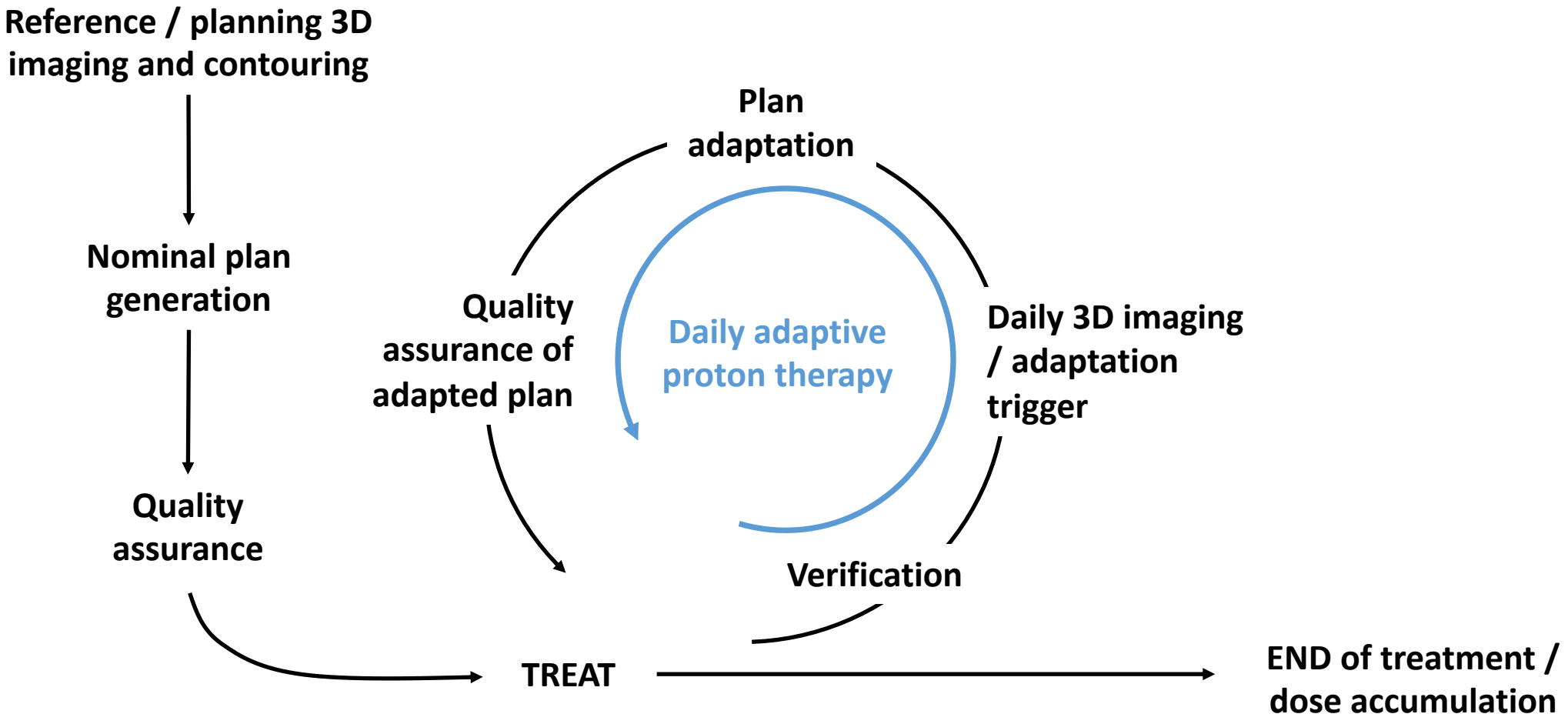


TREAT

Fractionated proton treatment course

END of treatment

Introduction – Adaptive Proton Therapy



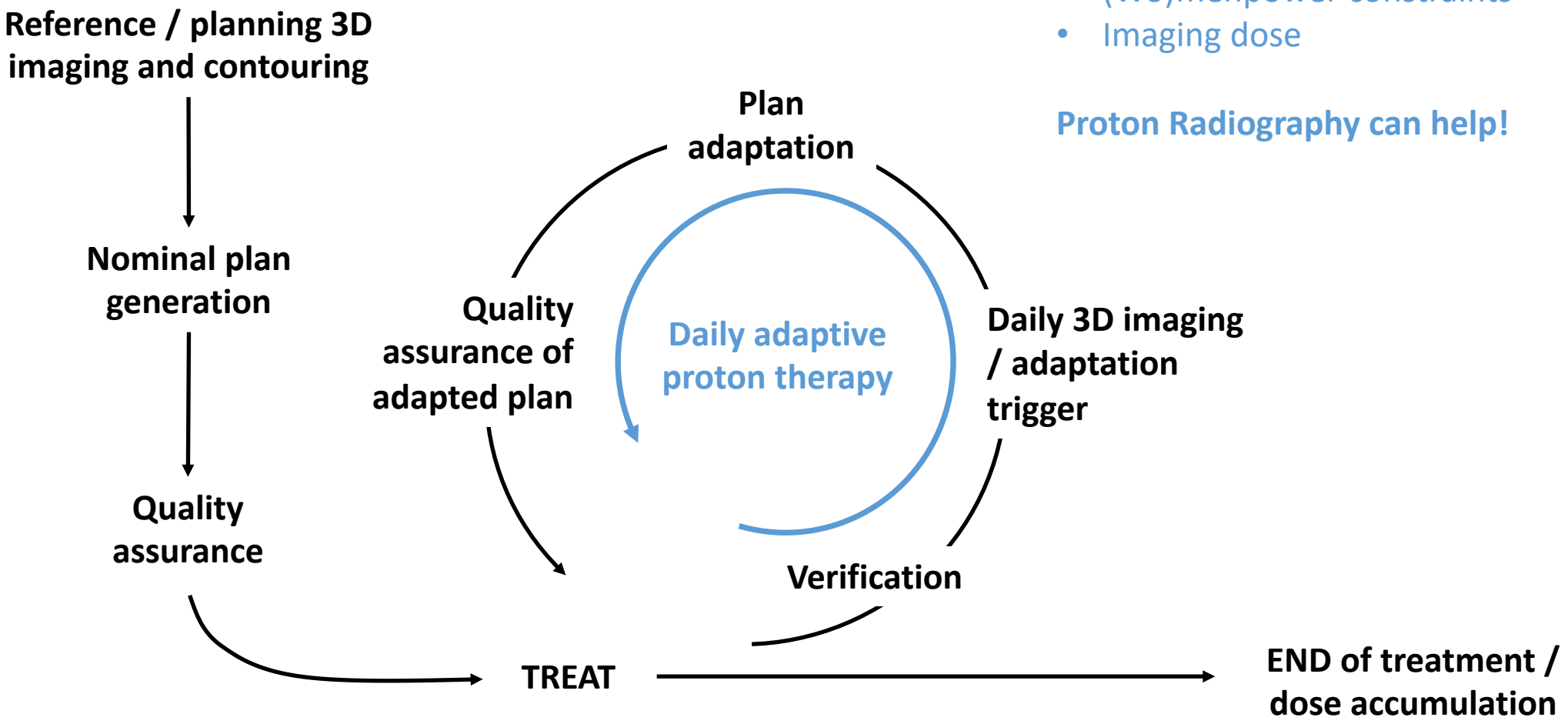
Albertini F, Matter M, Nenoff L, Zhang Y, Lomax A. **„Online daily adaptive proton therapy“**. Br J Radiol. 2020 Mar;93(1107):20190594. doi: 10.1259/bjr.20190594. Epub 2019 Nov 11. PMID: 31647313; PMCID: PMC7066958.

Introduction – Adaptive Proton Therapy

Challenges:

- Time constraints
- (Wo)menpower constraints
- Imaging dose

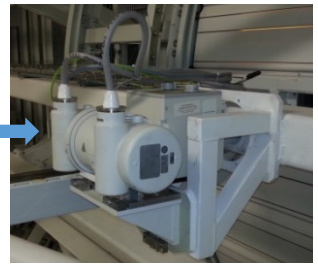
Proton Radiography can help!



Albertini F, Matter M, Nenoff L, Zhang Y, Lomax A. **„Online daily adaptive proton therapy“**. Br J Radiol. 2020 Mar;93(1107):20190594. doi: 10.1259/bjr.20190594. Epub 2019 Nov 11. PMID: 31647313; PMCID: PMC7066958.

Introduction – Proton Radiography

X-ray radiography



source
X-rays

object

detector
flat-panel

Proton radiography

source
p+ 230 MeV

object

detector
MLIC

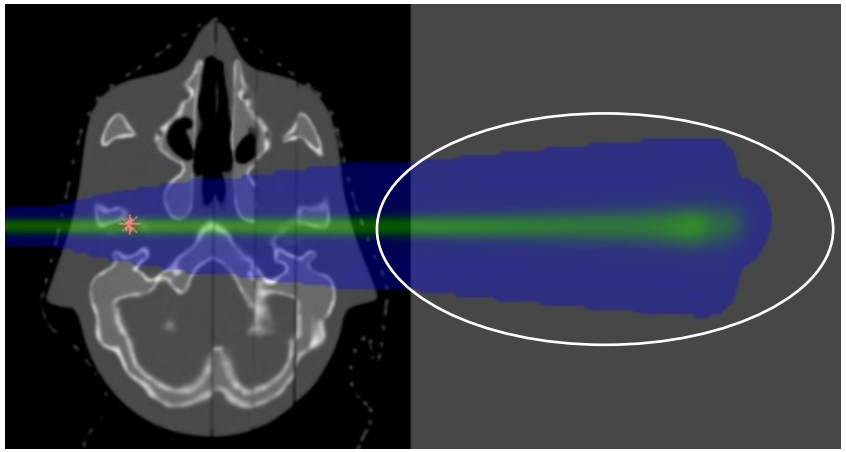
Introduction – Proton Radiography

X-rays

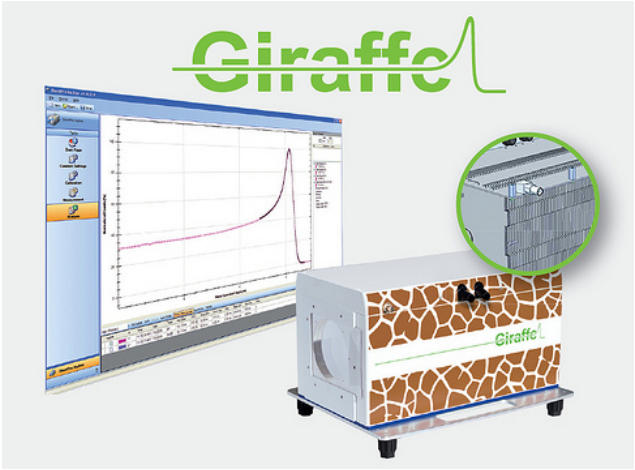
Protons

Methods – 2D range probe with MLIC

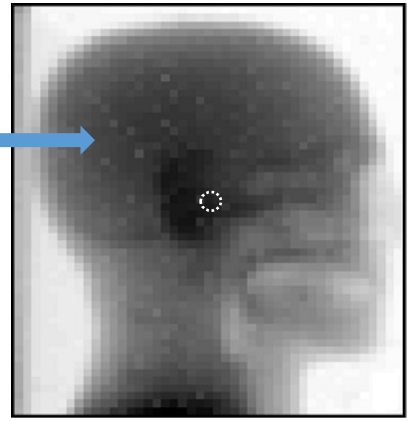
High energy (230 MeV)
Single pencil beam



Multilayer Ionization Chamber
(MLIC)

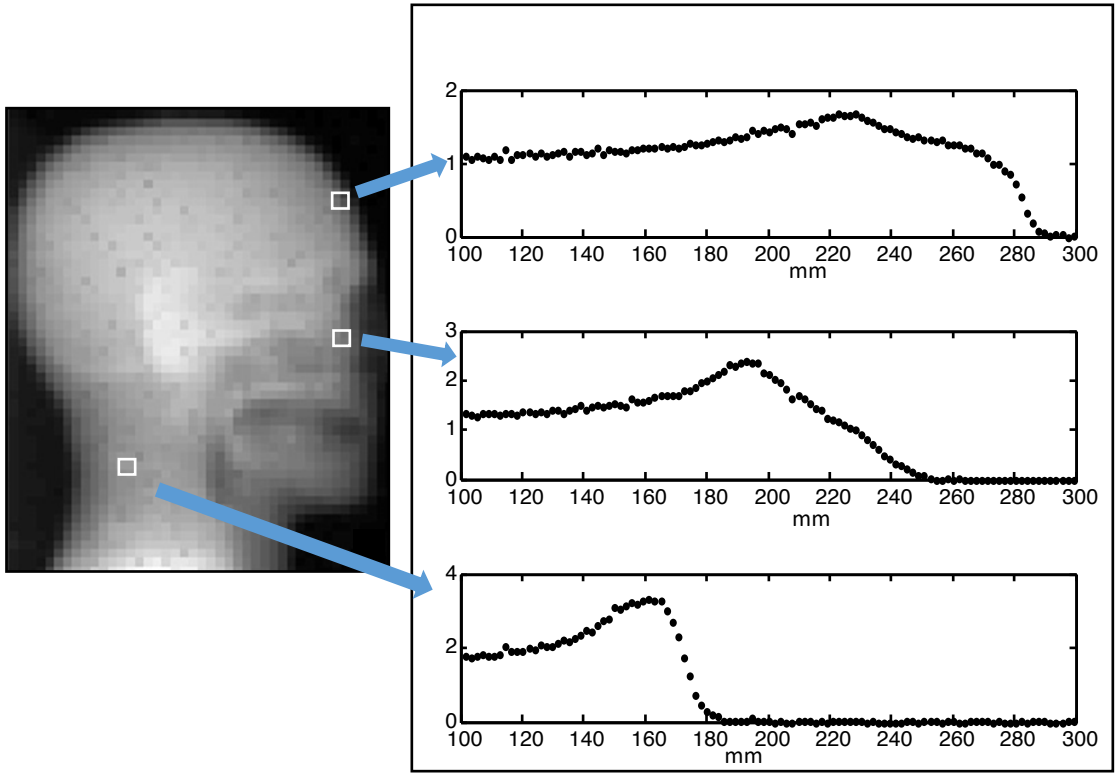


Integral Depth Dose
(IDD)



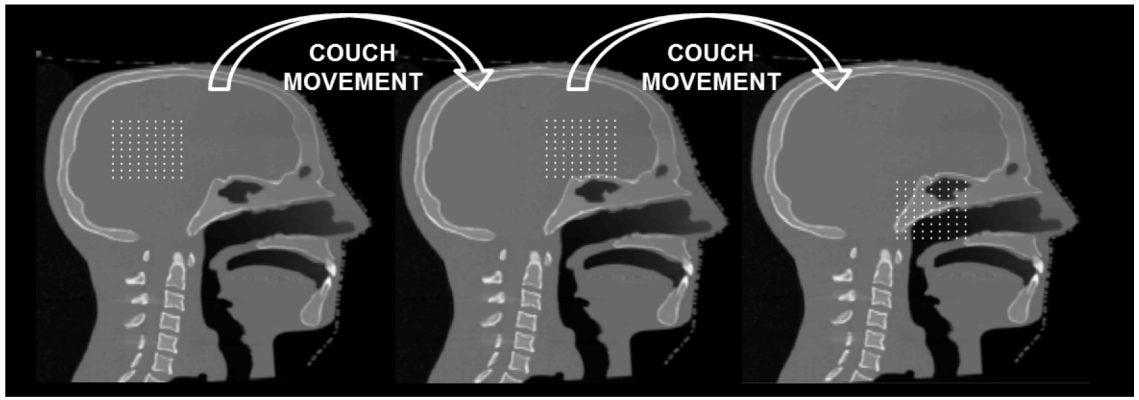
Methods – 2D range probe with MLIC

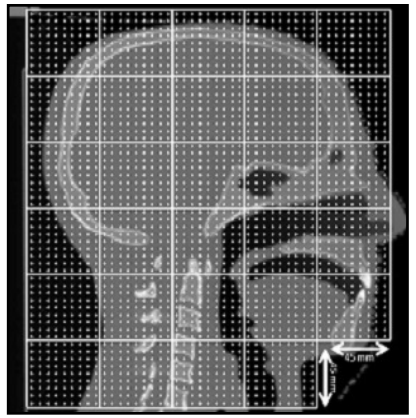
Pencil beam proton-radiography: More than a simple image !



Behind each pixel resides a residual IDD

Methods – 2D range probe with MLIC





SINGLE FRAME

Field of view:	45 x 45 mm
Spot matrix:	9 x 9 (81 spots)
Spot spacing:	5 mm
Beam-on time:	2.4 sec

BETWEEN FRAMES

about 45 sec
for couch movement,
and beam loading

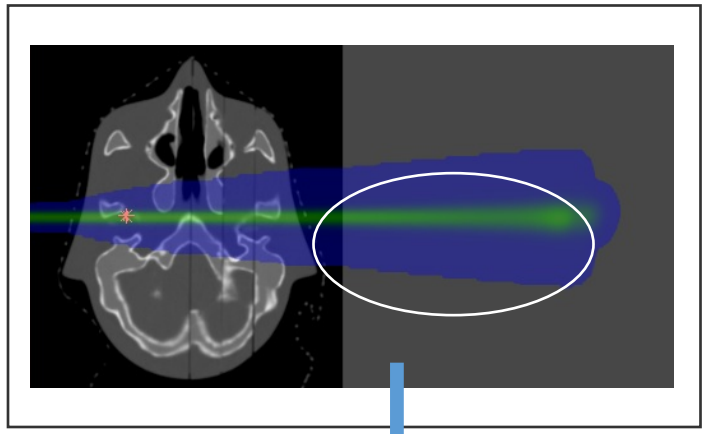
DOSE (TPS)

Maximum < 2 cGyE
Mean < 1 cGyE

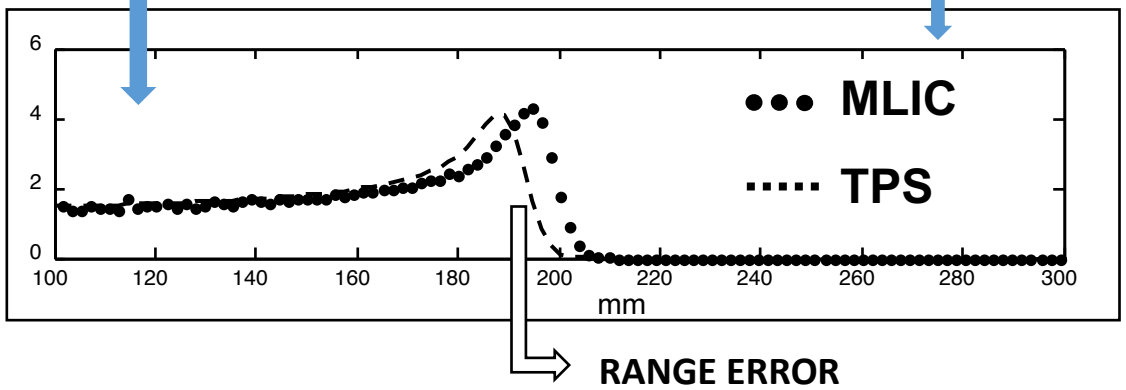
TOTAL TIME : for 30 frames, full head: 22min (110 s beam on)

Methods – 2D range probe with MLIC

MLIC Measurements



TPS calculation



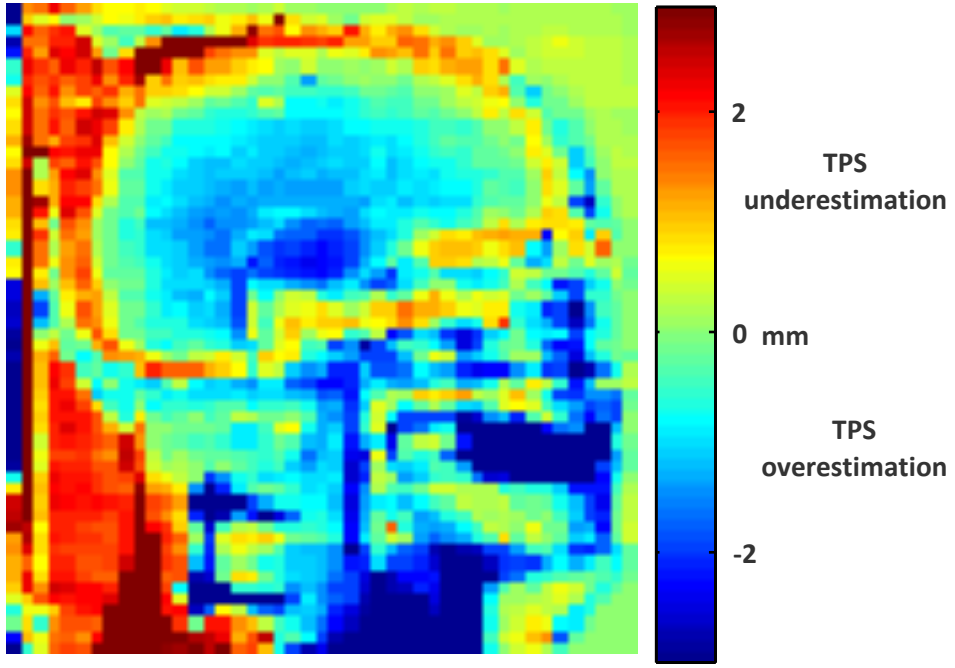
Applications

- Range error
- Classification of sources of range error
- Clinical quality control tool
- sCT quality control

Applications – Range error

RANGE ERROR MAP
(TPS prediction vs MLIC measurements)

PROTON RADIOGRAPHY

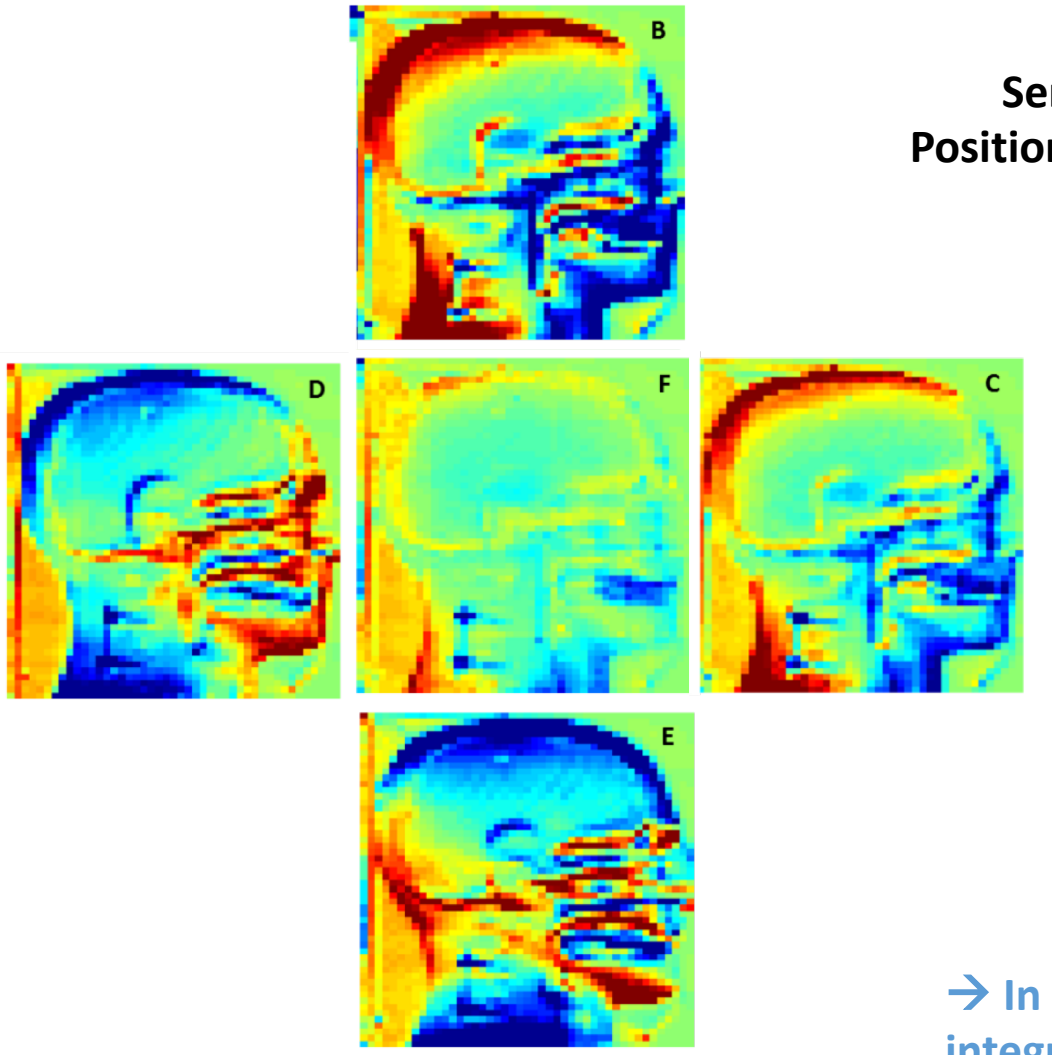


<u>Potential sources of errors :</u>

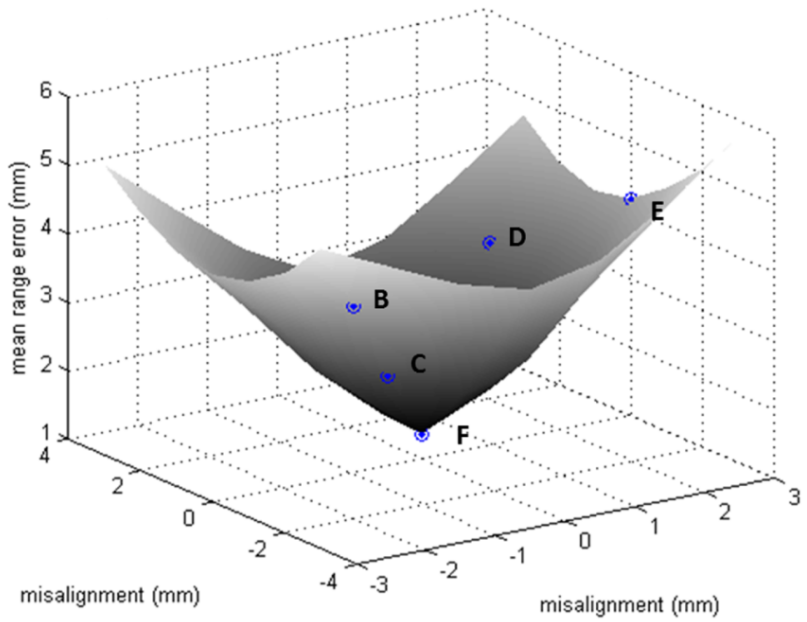
- Immobilization devices
- Titanium implants
- Misalignment

Farace P, Righetto R, Deffet S, Meijers A, Vander Stappen F. „**Technical Note: A direct ray-tracing method to compute integral depth dose in pencil beam proton radiography with a multilayer ionization chamber**“. Med Phys. 2016 Dec;43(12):6405. doi: 10.1118/1.4966703. PMID: 27908151.

Applications – Range error



Sensitivity to
Position misalignment

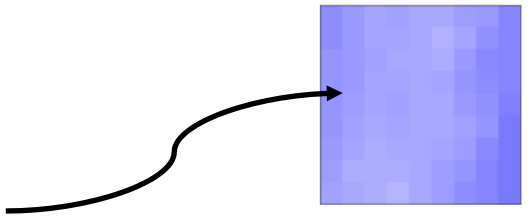


→ In an adaptive workflow, PR could be used as integrated quality control / verification tool

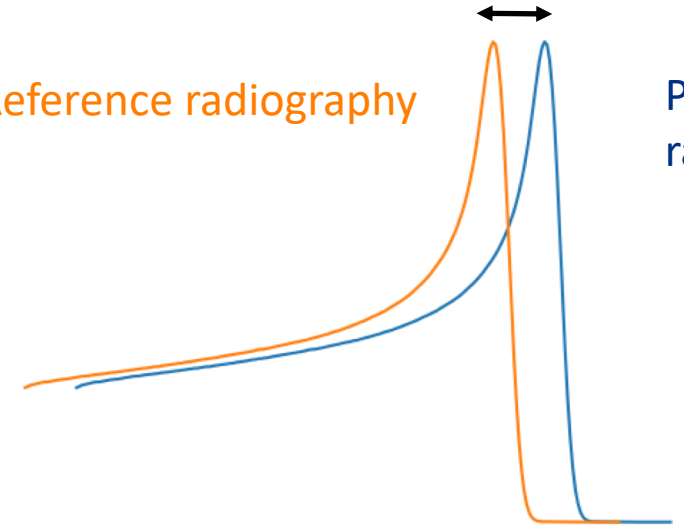
Farace P, Righetto R, Deffet S, Meijers A, Vander Stappen F. „**Technical Note: A direct ray-tracing method to compute integral depth dose in pencil beam proton radiography with a multilayer ionization chamber**“. Med Phys. 2016 Dec;43(12):6405. doi: 10.1118/1.4966703. PMID: 27908151.

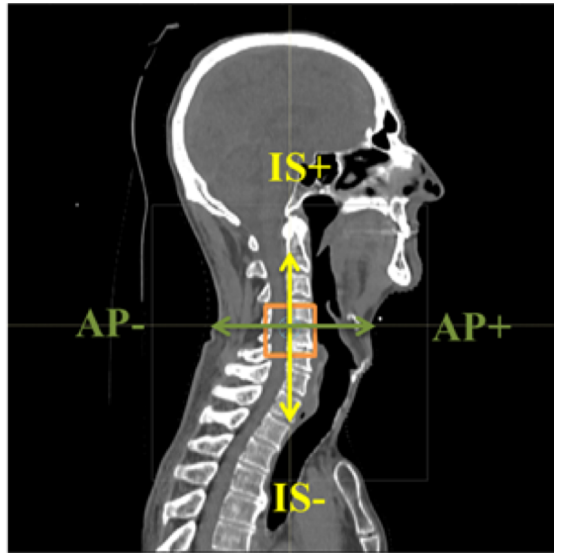
Applications – Classification of sources of range error

Deconvolution of uncertainties with proton radiography



RANGE SHIFT





soft, bone, fat HU perturbation

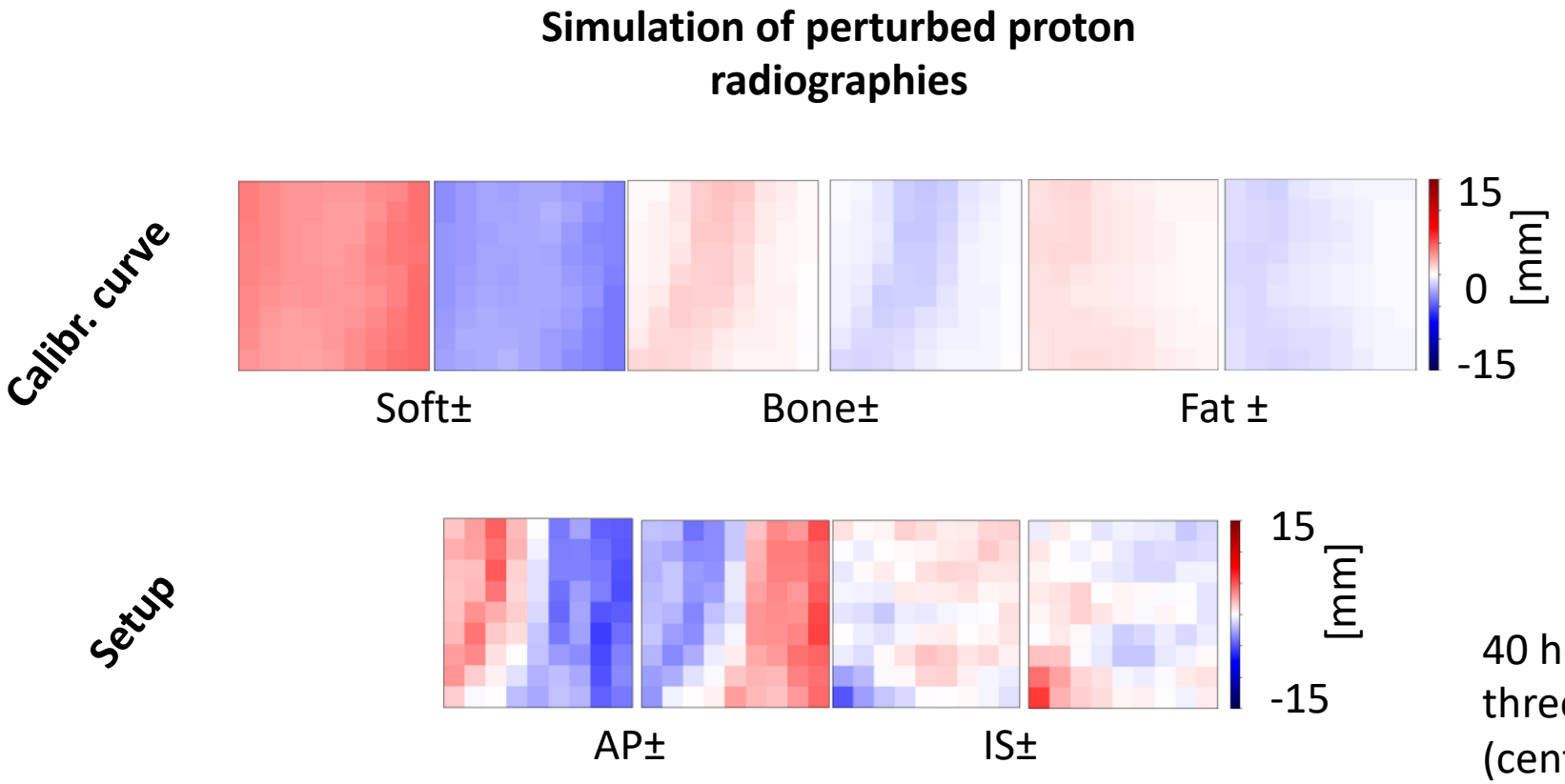
<u>Simulation study considering the following uncertainties:</u>

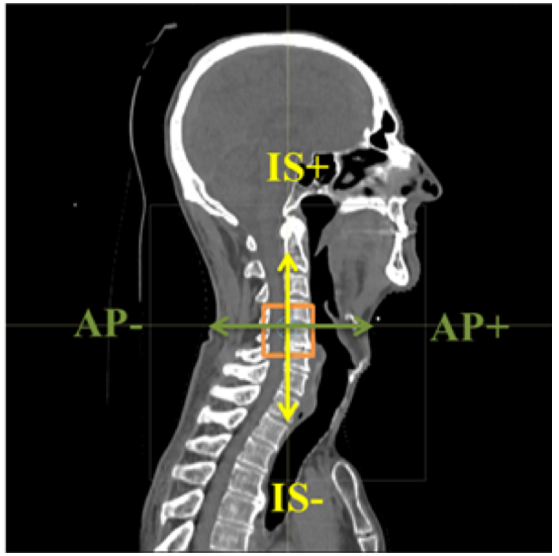
- Calibartion curve
- Setup errors

Individually and in combination

Oria CS, Marmitt GG, Both S, Langendijk JA, Knopf AC, Meijers A. „**Classification of various sources of error in range assessment using proton radiography and neural networks in head and neck cancer patients**“. Phys Med Biol. 2020 Nov 20;65(23). doi: 10.1088/1361-6560/abc09c. PMID: 33049722.

Applications – Classification of sources of range error





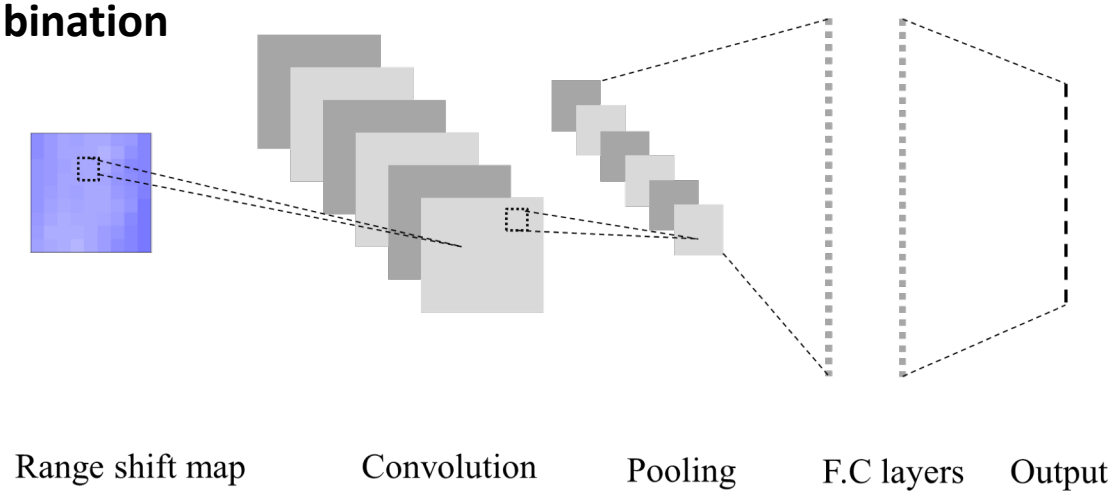
soft, bone, fat HU perturbation

40 head and neck cancer patients, at three different anatomical locations (centered for head and neck, neck and base of skull coverage)

Oria CS, Marmitt GG, Both S, Langendijk JA, Knopf AC, Meijers A. „**Classification of various sources of error in range assessment using proton radiography and neural networks in head and neck cancer patients**“. Phys Med Biol. 2020 Nov 20;65(23). doi: 10.1088/1361-6560/abc09c. PMID: 33049722.

Applications – Classification of sources of range error

CNN classifier: detection of different sources of uncertainty individually and in combination



Results

Individual uncertainties: 100% correct detection

Combinations: 73 % correct detection
27% partial detection

PR can distinguish between different sources of uncertainty

→ In an adaptive workflow, PR could be used to assist with adaptation triggering

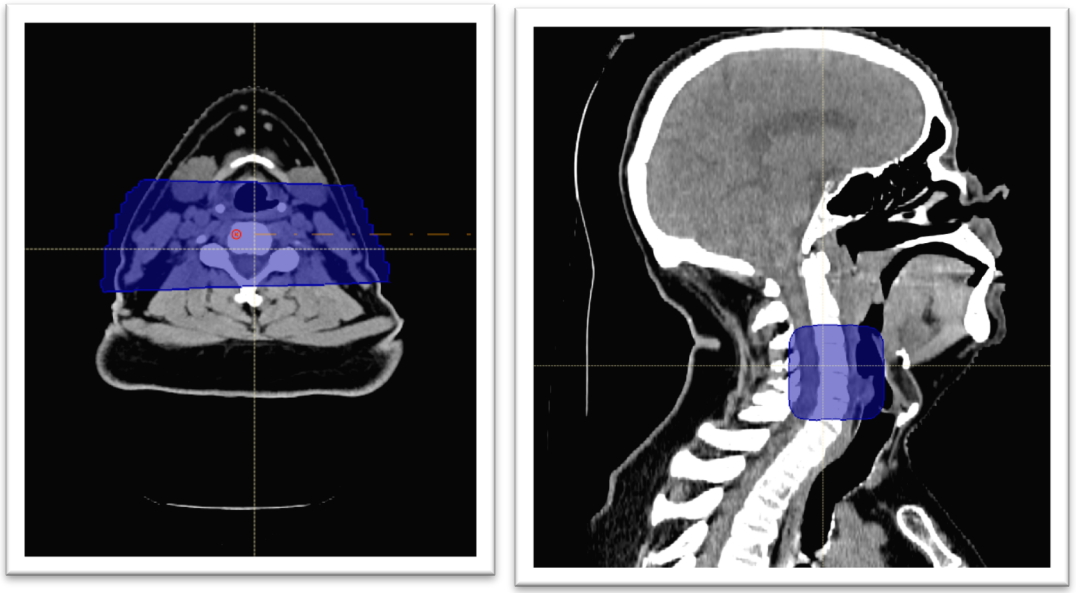
Oria CS, Marmitt GG, Both S, Langendijk JA, Knopf AC, Meijers A. „**Classification of various sources of error in range assessment using proton radiography and neural networks in head and neck cancer patients**“. Phys Med Biol. 2020 Nov 20;65(23). doi: 10.1088/1361-6560/abc09c. PMID: 33049722.

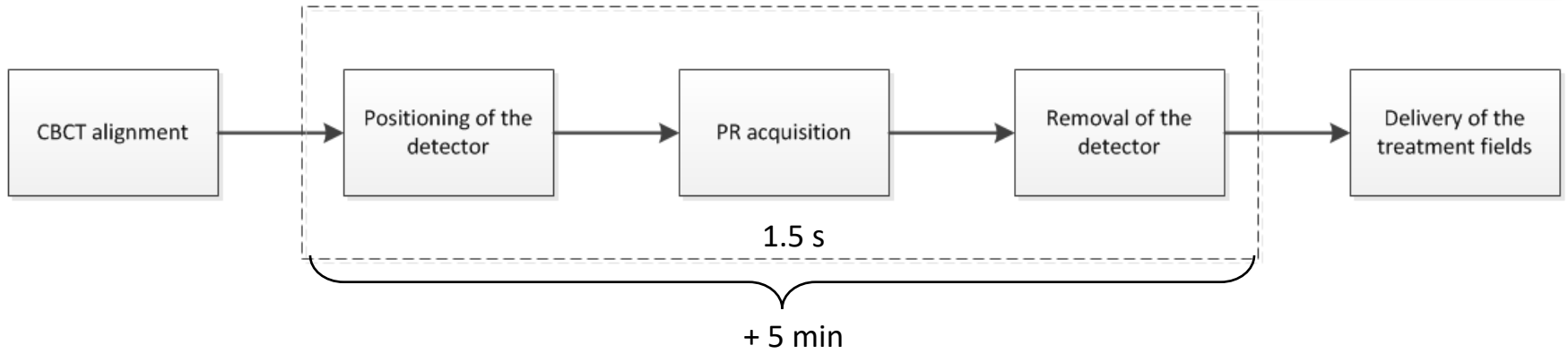
Applications – Clinical quality control procedure

Confirmation of the accuracy of CT based model on patient specific basis

PR field:
Area covered by 81 probe beam
Small size (4 x 4 cm^2)
Low dose (1.5 cGy)

Spots intersect mix of tissues:
Bony tissue
Soft tissue (fat, muscle, marrow)



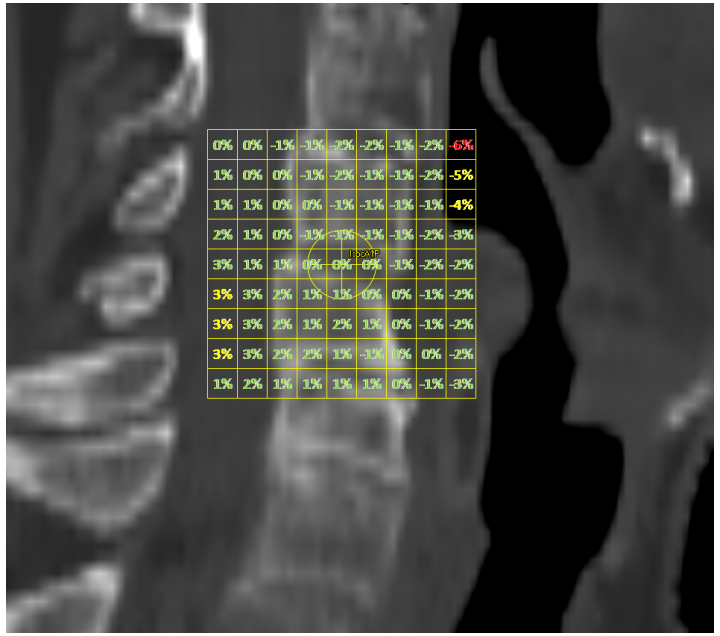


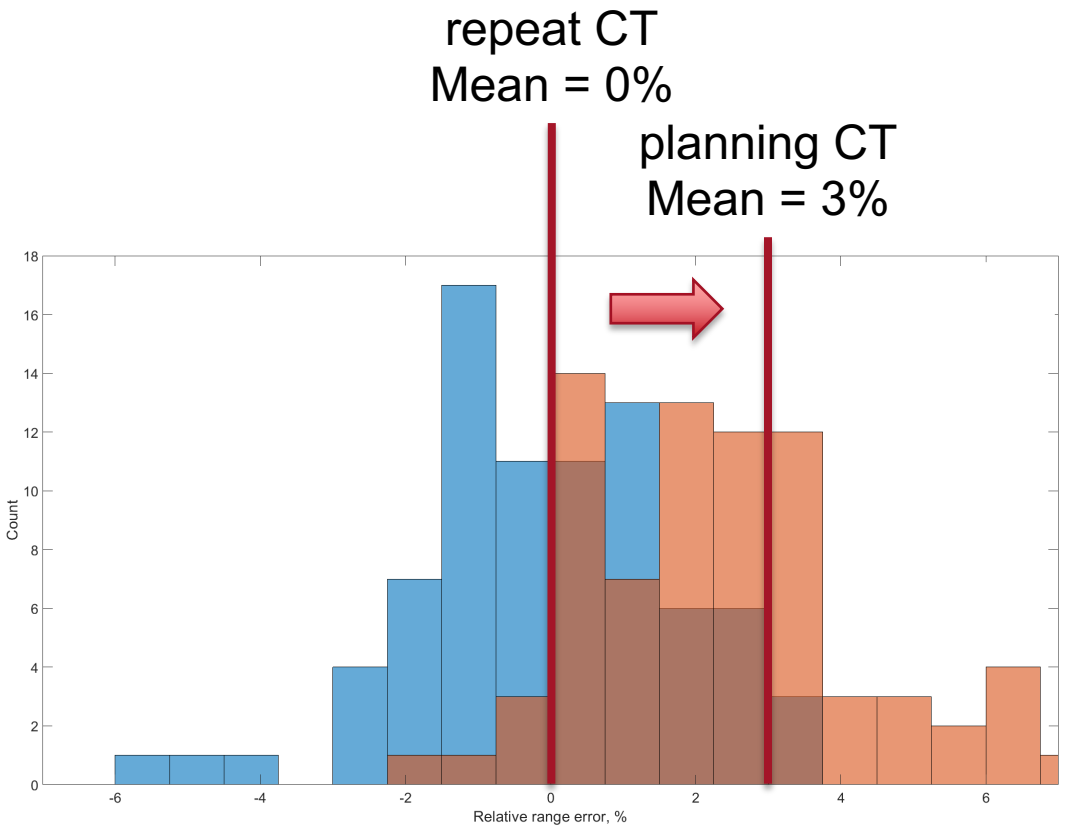
7 head and neck cancer patients, two RP frames were acquired within the first two weeks of treatment, on days when a repeated CT scan was obtained.

Meijers A, Seller Oria C, Free J, Langendijk JA, Knopf AC, Both S. **Technical Note: First report on an in vivo range probing quality control procedure for scanned proton beam therapy in head and neck cancer patients.** Med Phys. 2021 Mar;48(3):1372-1380. doi: 10.1002/mp.14713. Epub 2021 Feb 6. PMID: 33428795.

Applications – Clinical quality control procedure

repeat CT





The agreement of measured and simulated proton ranges confirms the 3% uncertainty margin for robust optimization.

Anatomical variations show a predominant effect on range accuracy, motivating efforts towards the implementation of adaptive radiotherapy.

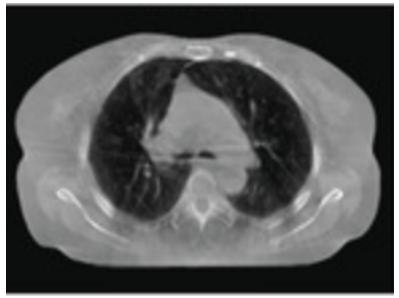
→ **In an adaptive workflow, PR could assist quality assurance**

Meijers A, Seller Oria C, Free J, Langendijk JA, Knopf AC, Both S. **Technical Note: First report on an in vivo range probing quality control procedure for scanned proton beam therapy in head and neck cancer patients.** Med Phys. 2021 Mar;48(3):1372-1380. doi: 10.1002/mp.14713. Epub 2021 Feb 6. PMID: 33428795.

Applications – sCT quality control

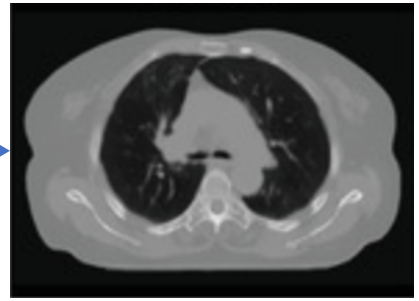
The cornerstone of adaptive workflows are daily images. Modern PT rooms are equipped with CBCT

CBCT



Imaging in treatment position, however wrong HU and image artefacts

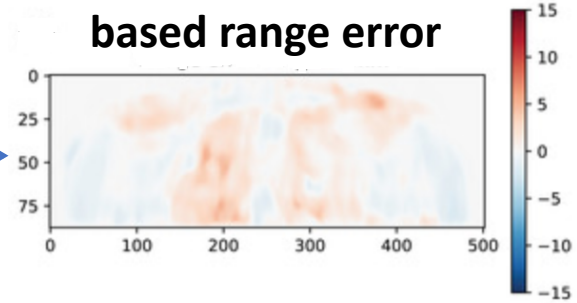
sCT



Correct HU? Artefacts ?

Correction DCNN

Proton radiography based range error



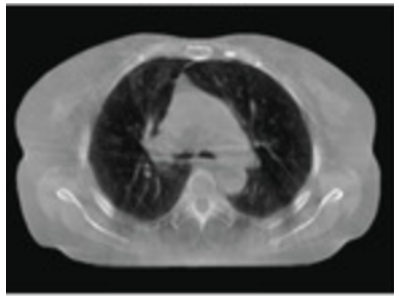
Thummerer A, Seller Oria C, Zaffino P, Meijers A, Guterres Marmitt G, Wijsman R, Seco J, Langendijk JA, Knopf AC, Spadea MF, Both S. **Clinical suitability of deep learning based synthetic CTs for adaptive proton therapy of lung cancer.** Med Phys. 2021 Dec;48(12):7673-7684. doi: 10.1002/mp.15333. Epub 2021 Nov 16. PMID: 34725829; PMCID: PMC9299115.

Seller Oria C, Thummerer A, Free J, Langendijk JA, Both S, Knopf AC, Meijers A. „**Range probing as a quality control tool for CBCT-based synthetic CTs: In vivo application for head and neck cancer patients“.** Med Phys. 2021 Aug;48(8):4498-4505. doi: 10.1002/mp.15020. Epub 2021 Jul 11. PMID: 34077554; PMCID: PMC8456797.

Applications – sCT quality control

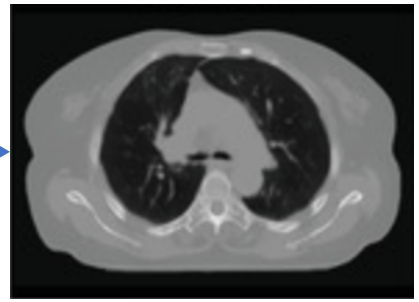
The cornerstone of adaptive workflows are daily images. Modern PT rooms are equipped with CBCT

CBCT



Imaging in treatment position, however wrong HU and image artefacts

sCT

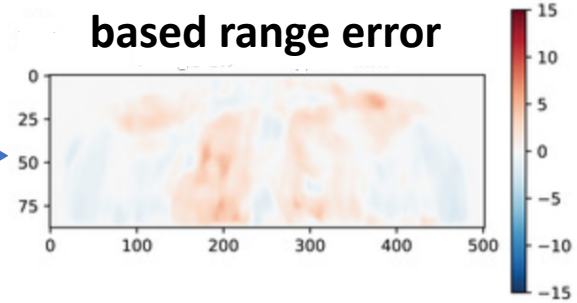


Correct HU
Artefacts ✓

Correction DCNN

Dose calculation → Plan adaptation

Proton radiography based range error



→ Details Carmen Seller

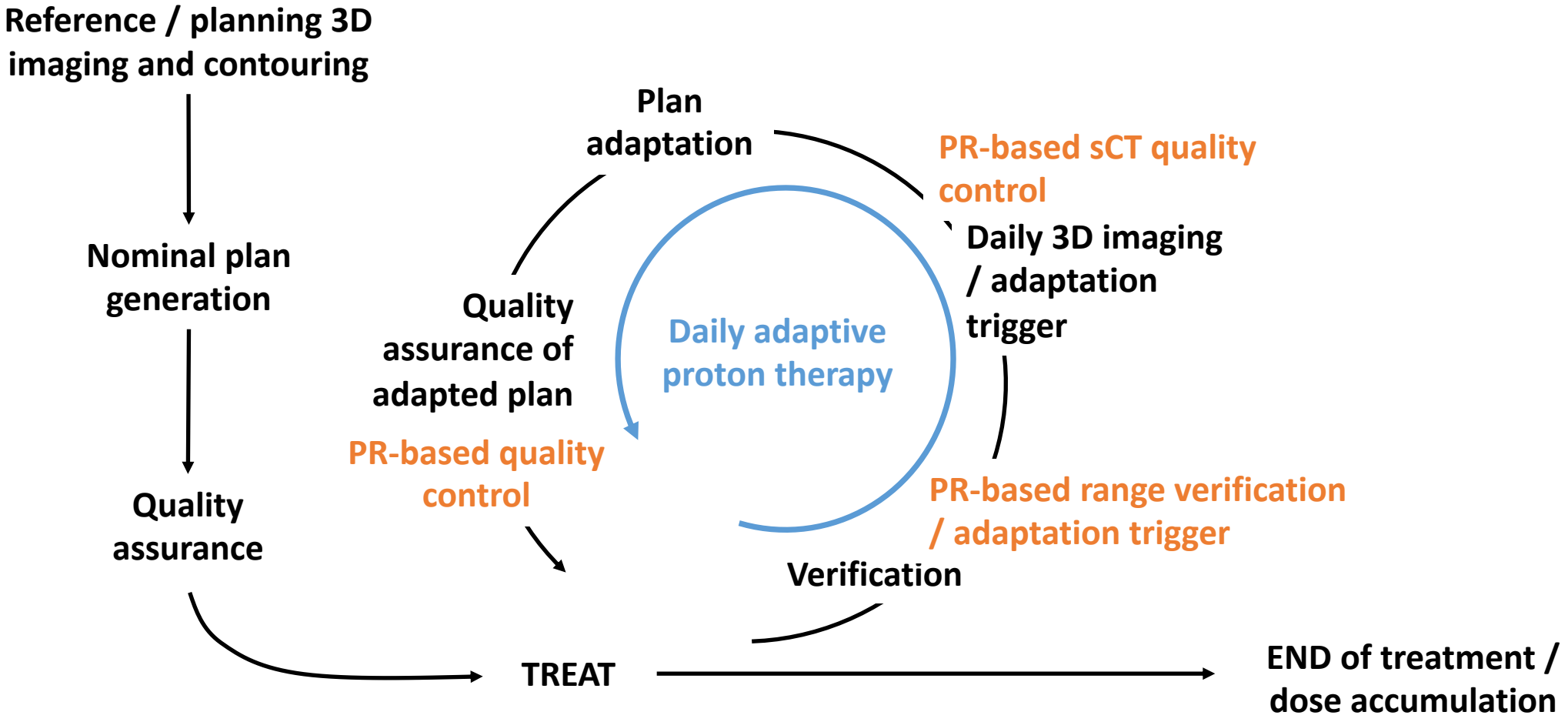
→ In an adaptive workflow, PR enables CBCT-based dose calculation and therby enables to spare imaging dose

Thummerer A, Seller Oria C, Zaffino P, Meijers A, Guterres Marmitt G, Wijsman R, Seco J, Langendijk JA, Knopf AC, Spadea MF, Both S. **Clinical suitability of deep learning based synthetic CTs for adaptive proton therapy of lung cancer.** Med Phys. 2021 Dec;48(12):7673-7684. doi: 10.1002/mp.15333. Epub 2021 Nov 16. PMID: 34725829; PMCID: PMC9299115.

Seller Oria C, Thummerer A, Free J, Langendijk JA, Both S, Knopf AC, Meijers A. „**Range probing as a quality control tool for CBCT-based synthetic CTs: In vivo application for head and neck cancer patients“.** Med Phys. 2021 Aug;48(8):4498-4505. doi: 10.1002/mp.15020. Epub 2021 Jul 11. PMID: 34077554; PMCID: PMC8456797.

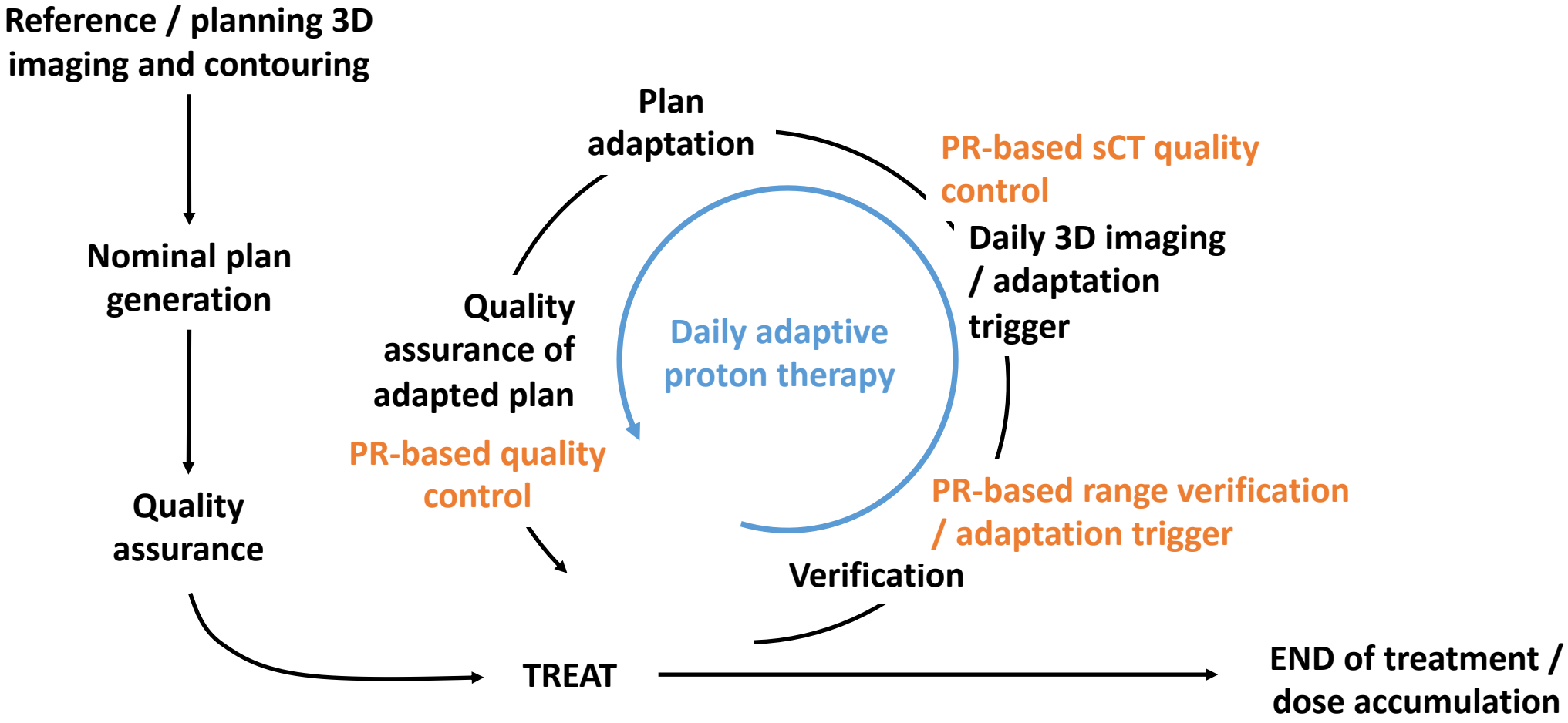
Conclusion

Challenges:
- Time constraints
- (Wo)menpower constraints
- Imaging dose



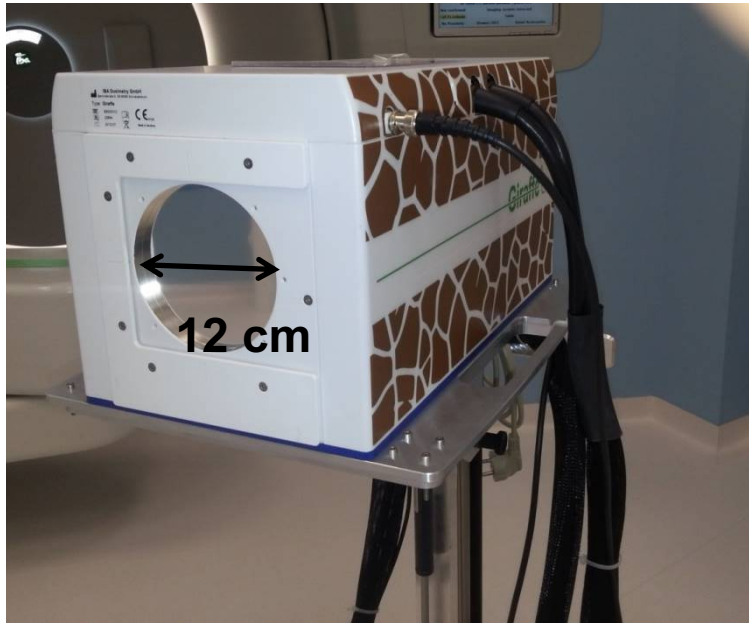
Conclusion

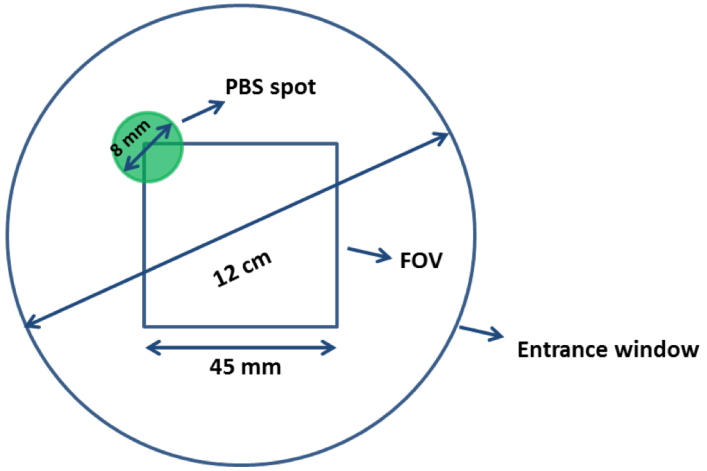
→ Proton radiography can help to overcome current challenges of daily adaptive proton therapy. It can be employed as quality control tool and has the potential to optimize adaptive workflows with respect to time, (wo)menpower and imaging dose.



Outlook

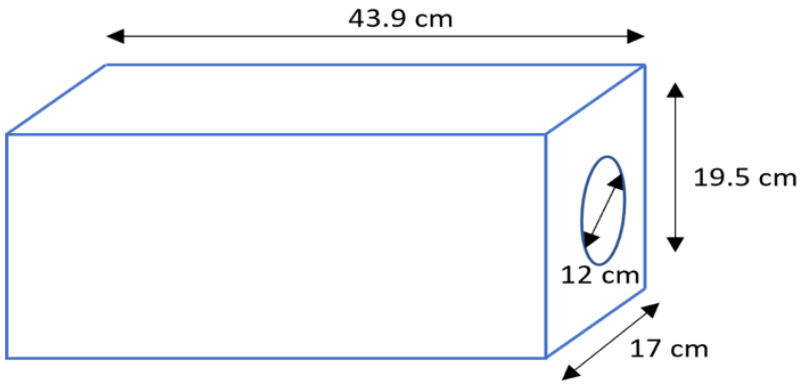
Detector refinement





Limited Field Of View

- Requires detector repositioning for bigger areas of interest



Extendet longitudinal dimension

- Impeds flexible detector positioning

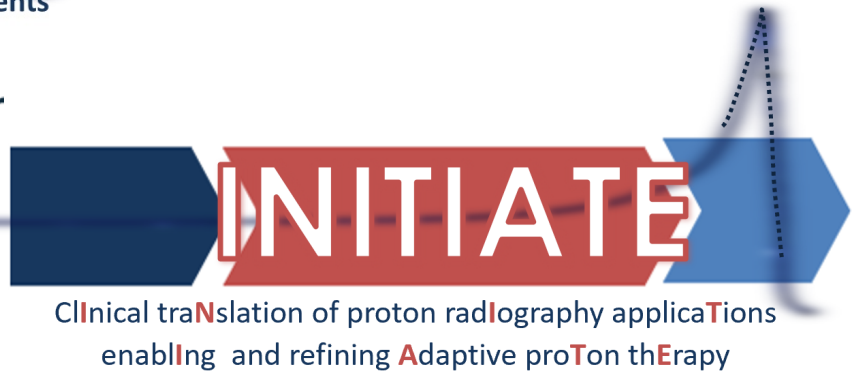
Outlook

Detector refinement

Optimized detector design would allow for:

- An improved integation of proton radiograpy in the clinical workflow
- An optimization of range pobing location
- Beams eye view (or at any angle) range probing

→ submitted



Outlook

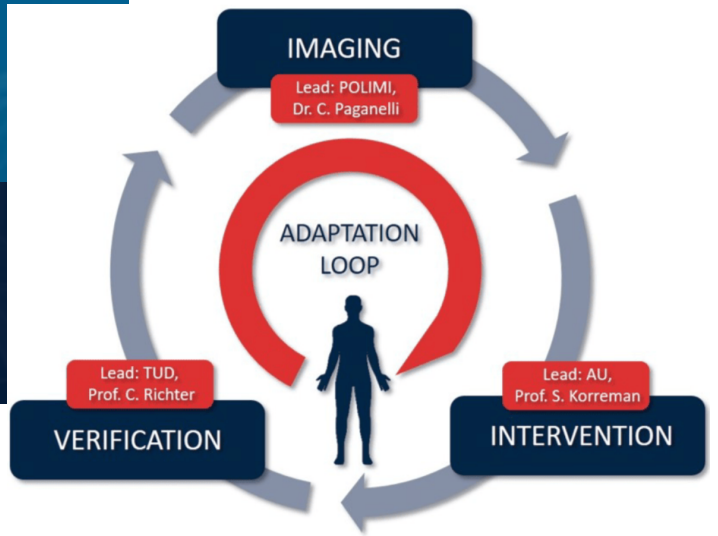
Proton Radiograpy is also part of RAPTOR

A MARIE SKŁODOWSKA-CURIE INNOVATIVE TRAINING NETWORK (ITN)

Real-Time Adaptive Particle Therapy Of Cancer (RAPTOR)

RAPTOR brings together 13 Beneficiaries and 15 partner organizations with one aim in common: To bring adaptive particle therapy to the clinic.

Funded by the Horizon 2020 Framework Programme of the EU.



Project 15
Giuliano Perotti Bernardini
Proton Radiography for real-time Intensity Modulated Proton Therapy plan adaptation

Proton Radiography for real-time Intensity Modulated Proton Therapy plan adaptation, Host: Cancer Research Center Groningen (CRCG) Research Institute of the UMCG, Netherlands.

Questions?
Thank you for your attention!

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KWF KANKER BESTRIJDING

INCONTROL
Clinical Control Infrastructure for Proton Therapy Treatments