AAPM COMP 2020

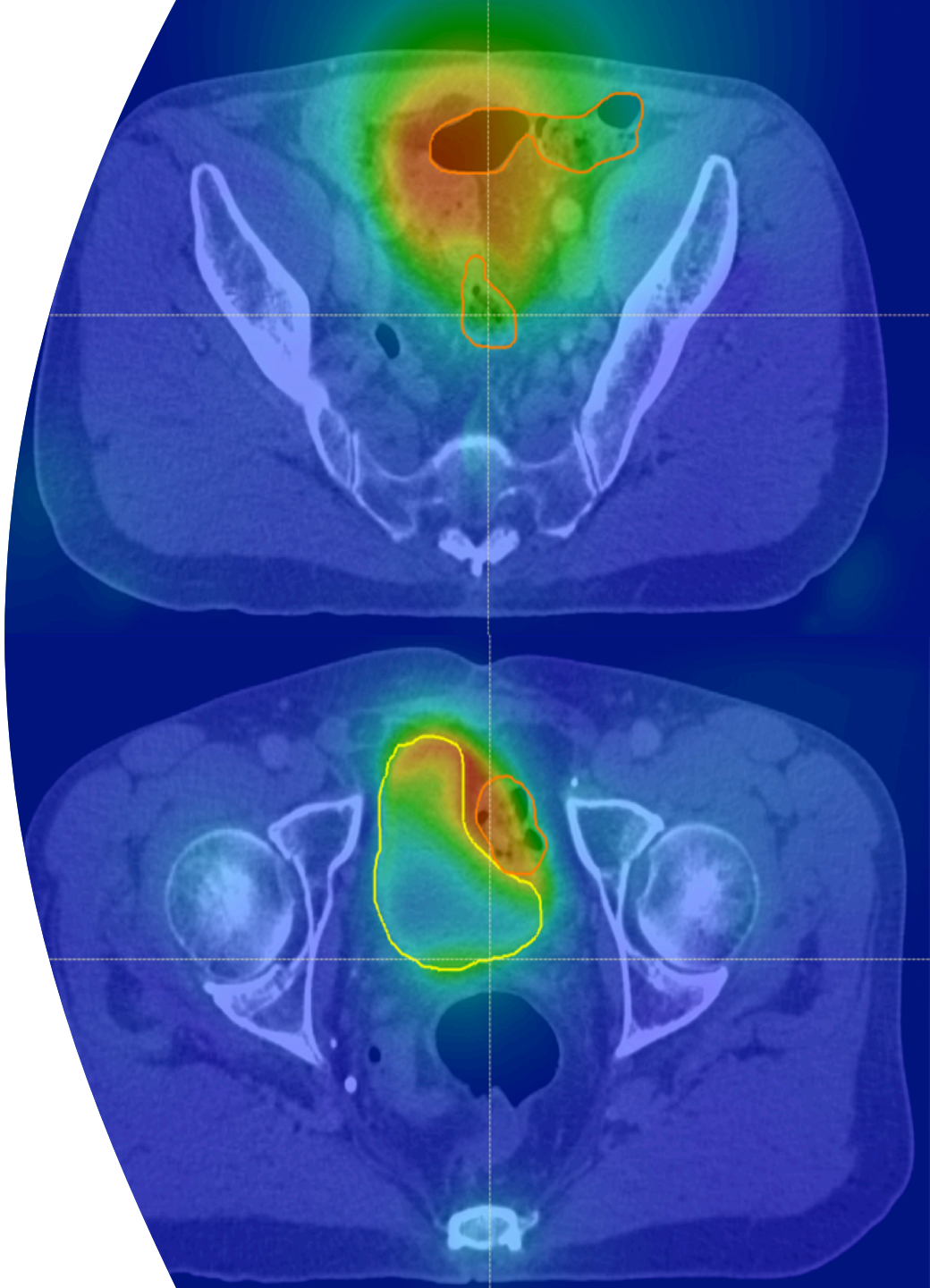
UK Approaches to ReIrradiation

SABR reirradiation with DIR and EQD2 optimisation

Ane Appelt

Associate Professor, University of Leeds, UK

@cancerphysicist



CANCER RESEARCH UK | RADNET LEEDS

Together we will beat cancer

DISCLOSURES

Employment

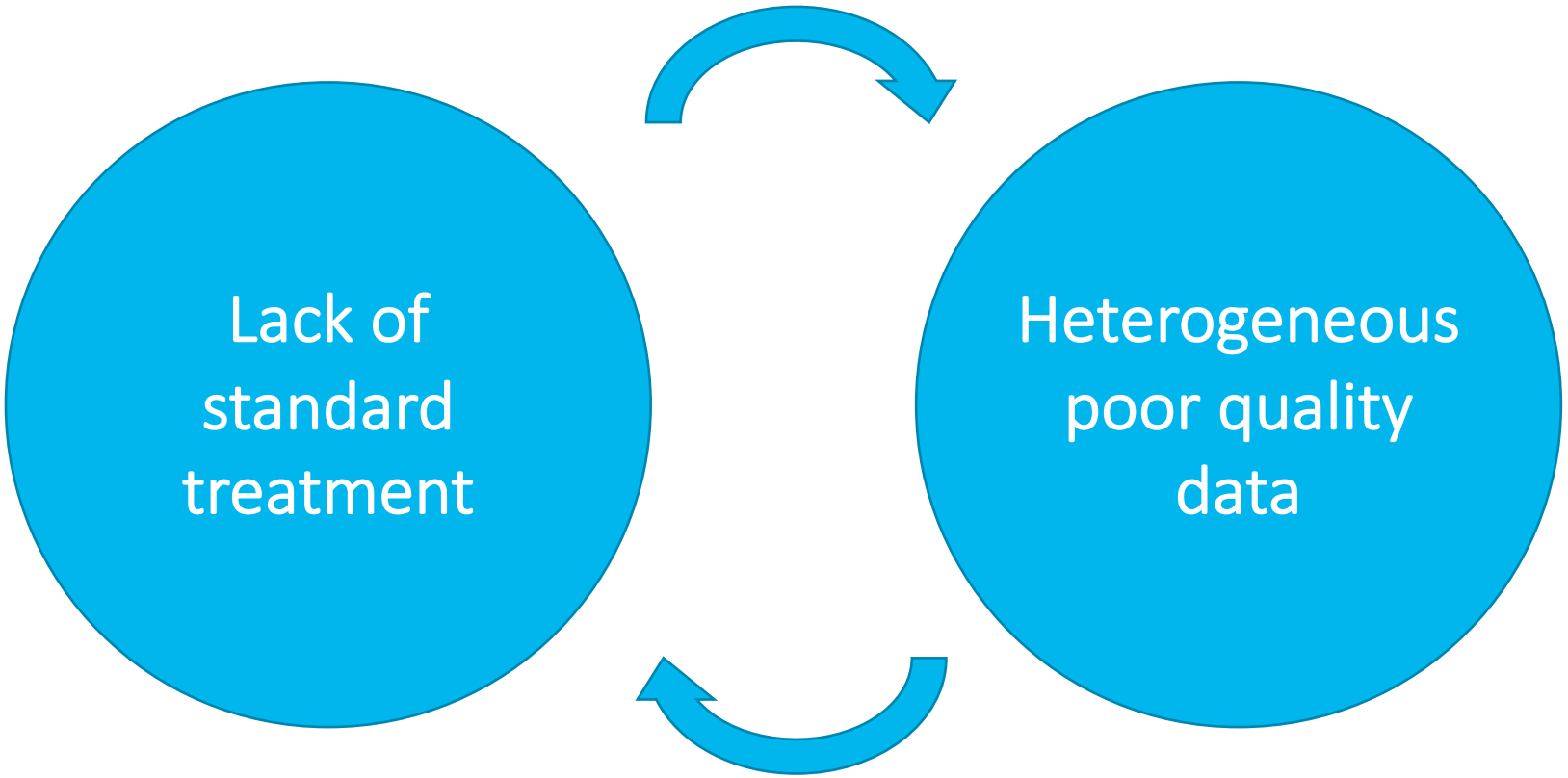
- University of Leeds
- Leeds Teaching Hospitals Trust

Research funding

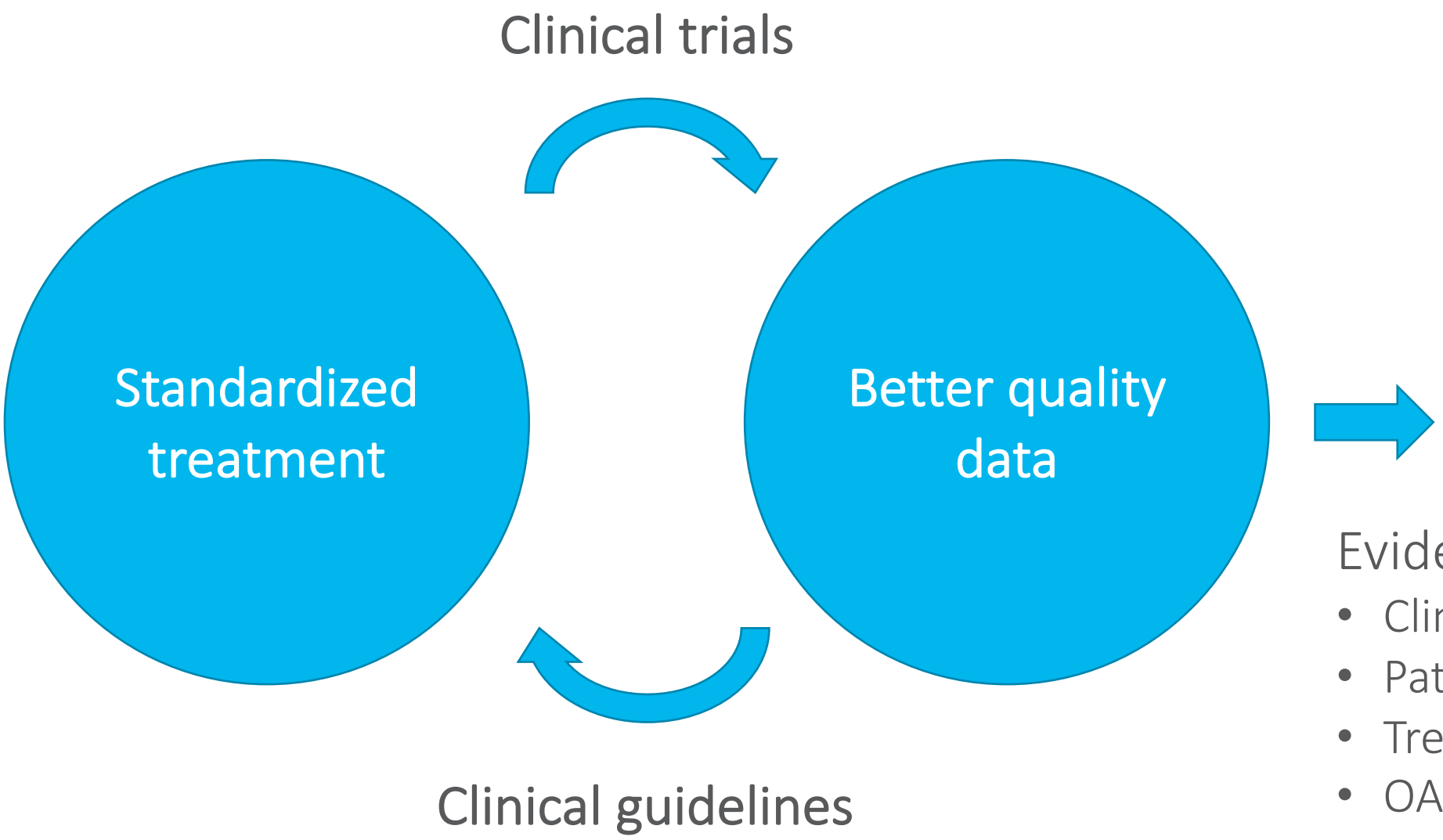
- Yorkshire Cancer Research
- Medical Research Council UK
- Cancer Research UK RadNet programme

Research collaboration agreement with RaySearch

EVIDENCE CHALLENGE IN REIRRADIATION



EVIDENCE CHALLENGE IN REIRRADIATION



Evidence for

- Clinical benefit
- Patient selection
- Treatment schedules
- OAR tolerance & repair

COMMISSIONING THROUGH EVALUATION (CtE)

"enables a limited number of patients to access treatments that are not funded by the NHS, but nonetheless show significant promise for the future, while new clinical and patient experience data are collected within a formal evaluation programme"

- Controlled access to treatments with limited evidence of benefit
- Standardised treatment in limited number of specialist centres
- Compulsory collection of data for evaluation

SABR reirradiation for pelvis and spine

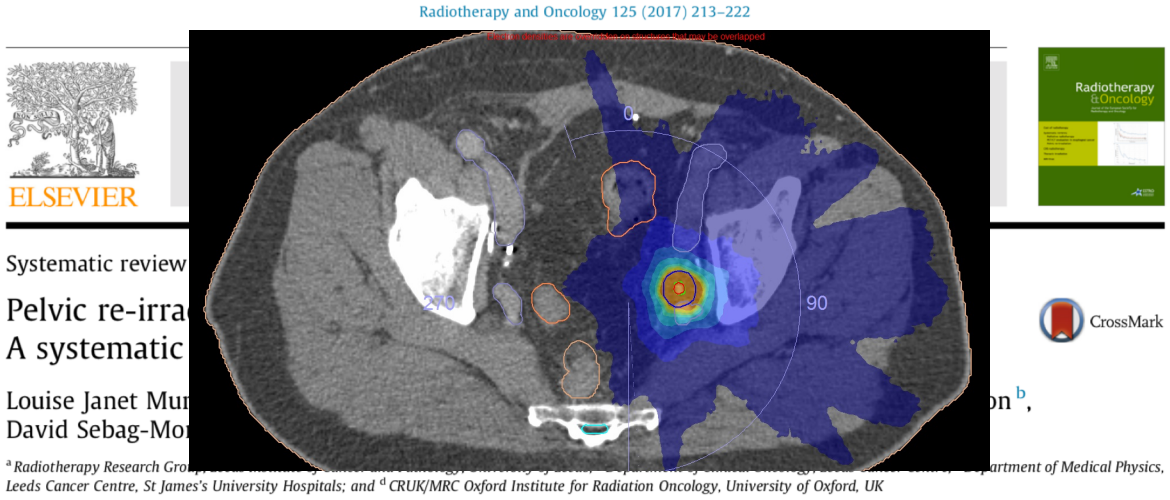
WHY PELVIC SABR REIRRADIATION?

Limited options for relapse in previously irradiated pelvis

- Surgery
  - Exenterative; frequent positive margins; many not suitable
- Systemic therapy
  - Suboptimal for localised problem; side effects; not curative
- Re-irradiation
  - Broadly avoided; usually hyperfractionated RT

SABR

- Highly focused, tight margins, rapid dose fall off
  - Less normal tissue irradiation
- High dose (better local control?)
- Few visits (better patient experience?)



CtE PATIENT SELECTION & TREATMENT

Patient selection:

- Life expectancy > 6 months
- > 6 months from initial radiotherapy
- No significant toxicity from previous radiotherapy
- Performance status 0-2; Ambulatory without severe co-morbidity

Up to 30 Gy in 5 fractions depending on previous dose

TREATMENT STANDARDISATION

8 centres treating with SABR reirradiation

Centralised collection of clinical, dose plan and imaging data

Gastrointestinal Constraints:

Description	Constraint	3 fraction		5 fraction	
		Optimal	Mandatory	Optimal	Mandatory
Duodenum	DMax (0.5cc)	-	< 22.2Gy	-	< 35Gy
	D1cc	-	-	< 33Gy	-
	D5cc	-	< 16.5Gy	< 25Gy	-
	D9cc	-	-	< 15Gy	-
	D10cc	-	< 11.4Gy	-	< 25Gy
Stomach	DMax (0.5cc)	-	< 22.2Gy	< 33Gy	< 35Gy
	D5cc	-	-	< 25Gy	-
	D10cc	-	< 16.5Gy	-	< 25Gy
	D50cc	-	-	< 12Gy	-
Small Bowel	DMax (0.5cc)	-	< 25.2Gy	< 30Gy	< 35Gy
	D5cc	-	< 17.7Gy	< 25Gy	-
	D10cc	-	-	-	< 25Gy
Oesophagus	DMax (0.5cc)	-	< 25.2Gy	< 32Gy	< 34Gy (Use <40 Gy for 8 fractions)
Large Bowel	DMax (0.5cc)	-	< 28.2Gy	-	< 32Gy
Common Bile Duct	DMax (0.5cc)	< 50Gy	-	< 50Gy	-
Parallel GI organs					
Normal Liver (Liver minus GTV)	V10Gy	-	-	< 70%	-
	Mean liver dose	-	-	< 13Gy	< 15.2Gy
	D50%	< 15Gy	-	-	-

General Pelvic Dose Constraints:

Description	Constraint	3 Fractions		5 Fractions	
		Optimal (Gy)	Mandatory (Gy)	Optimal (Gy)	Mandatory (Gy)
Bladder	D15cc	-	< 16.8	-	< 18.3
	DMax (0.5cc)	-	< 28.2	-	< 38
Penile Bulb	D3cc	-	< 21.9	-	< 30
	DMax (0.5cc)	-	< 42	-	< 50
Ureter	DMax (0.5cc)	-	< 40	-	< 45

CtE

NHS England

Commissioning through evaluation of stereotactic ablative radiotherapy (SABR): guidance on minimum technical standards

v1.01 8th July 2015

produced for NHS England
by the UK SABR Consortium,
and the Radiotherapy Trials QA Group

http://www.swscn.org.uk/wp/wp-content/uploads/2014/11/SABR-CtE-Service-Specification-2nd-Sept-2015-final.pdf

CtE SABR REIRRADIATION RESULTS

n=185 for pelvic re-irradiation

40% prostate cancer (+ anorectal cancer, gynaecological cancers)

Results not yet official (but anecdotally successful)

Leeds (Sept '18)

Patients:

- 34 patients
- Majority prostate patients (27/34)
- Mainly side wall nodes
  - On the edge of previous high dose region
- Median follow up 10.4 months

Local control

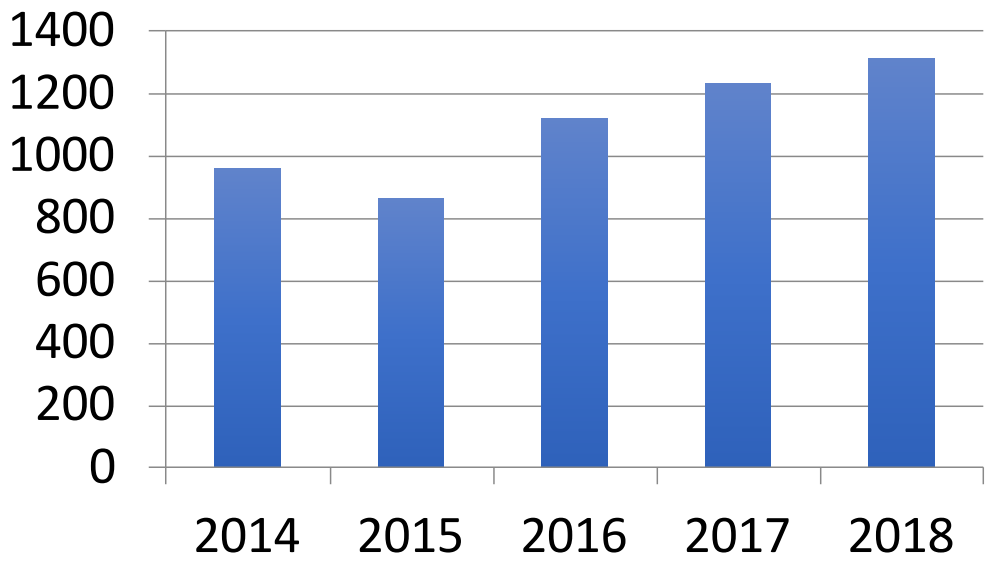
- 97% (imaging or PSA control)

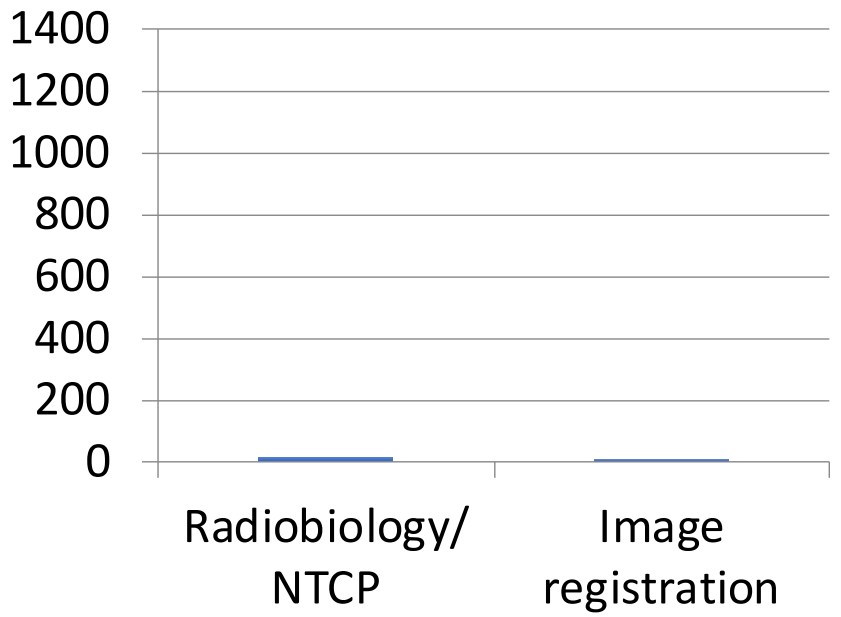
Out-of field:

- 42% out of field progression after median of 11.8 months (n=19 imaged)
- Median time to PSA failure: 14.5 months

One year survival 94%
Grade 1-2 acute fatigue, abdominal pain or diarrhea
No severe toxicities to date

SO IS THIS GOING TO SOLVE REIRRADIATION?

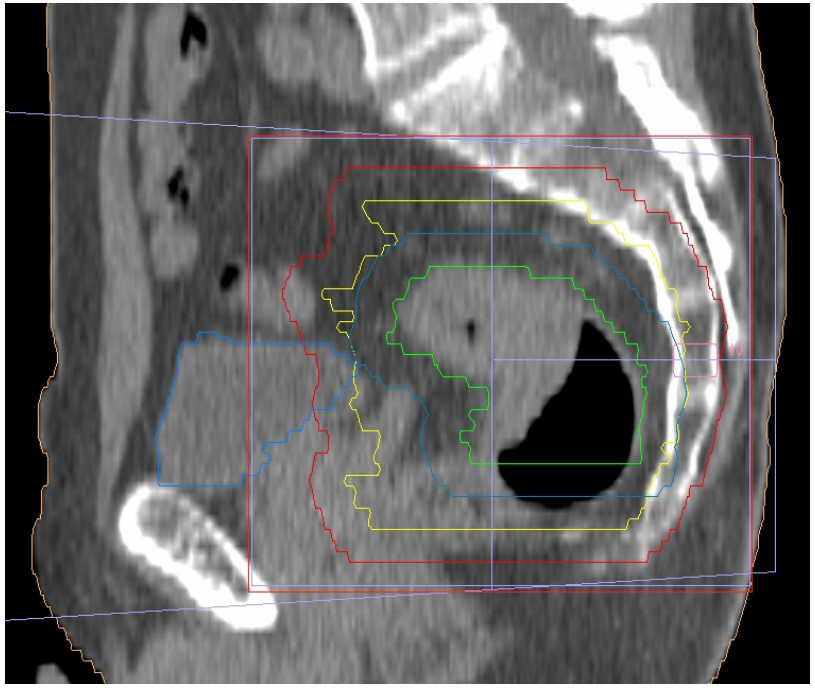




Reirradiation has not significantly benefitted from state-of-the-art developments in radiotherapy

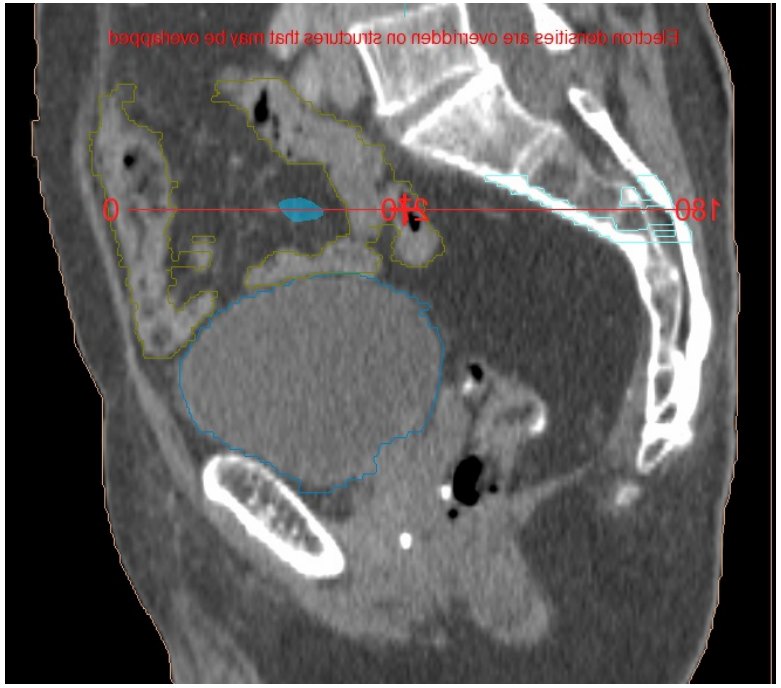
ANATOMICAL CHANGE – SPOT THE DIFFERENCE!

Former



Rectum / no pelvic surgery
Empty bladder

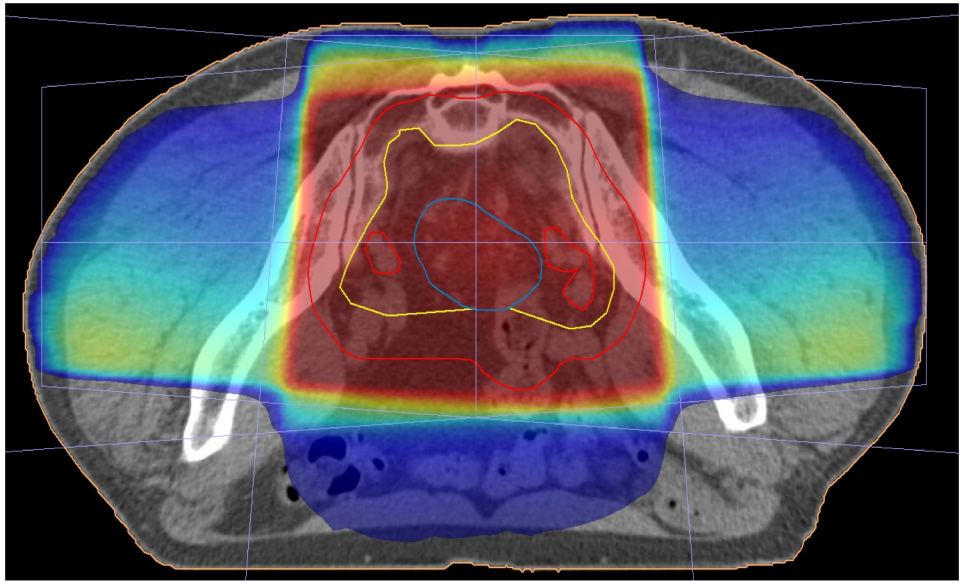
Reirradiation



No rectum / pelvic surgery
Fuller bladder

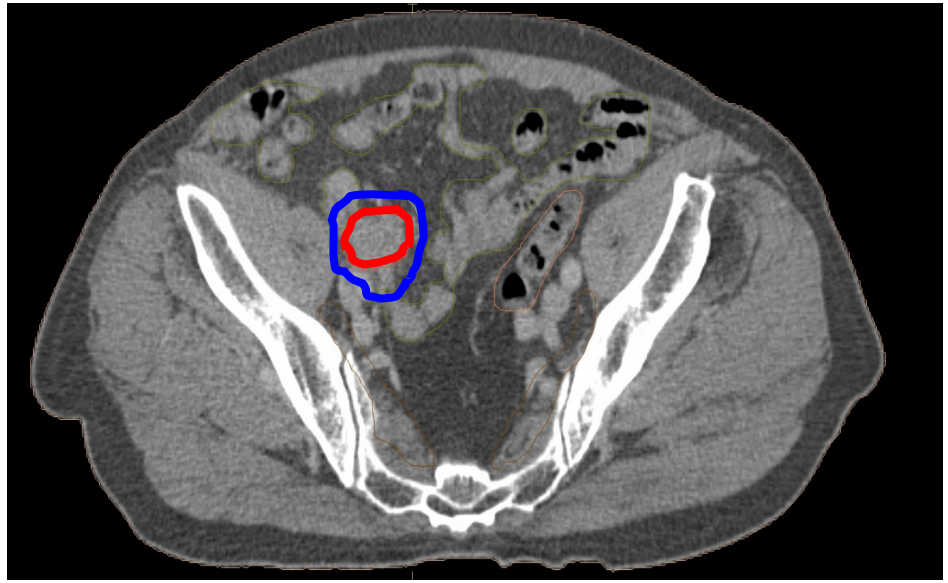
ANATOMICAL CHANGE – SPOT THE DIFFERENCE!

Former



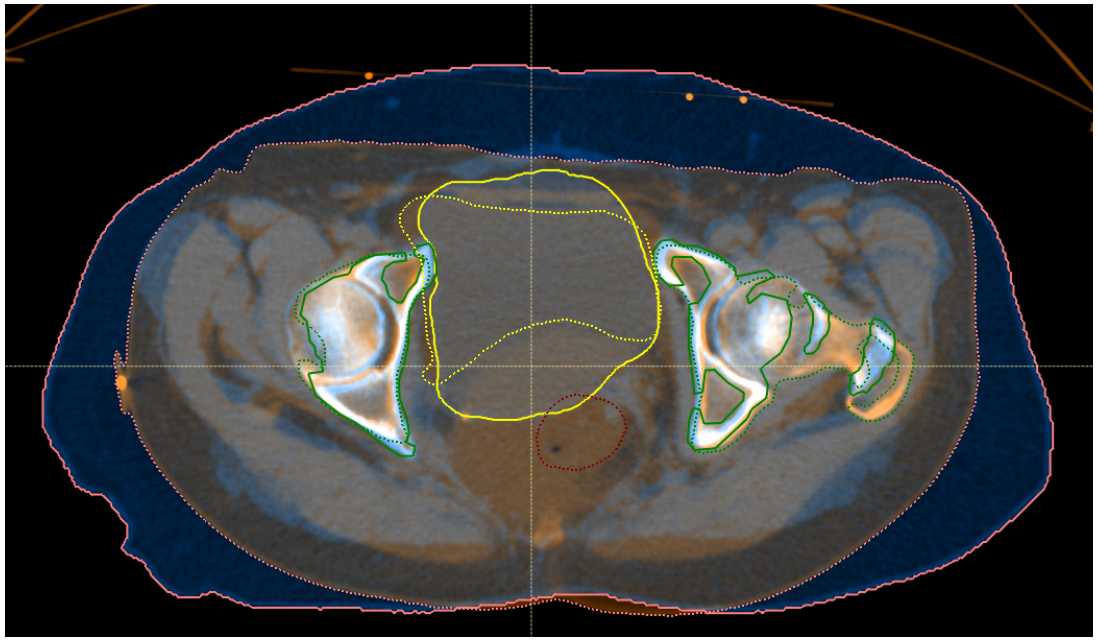
Prone

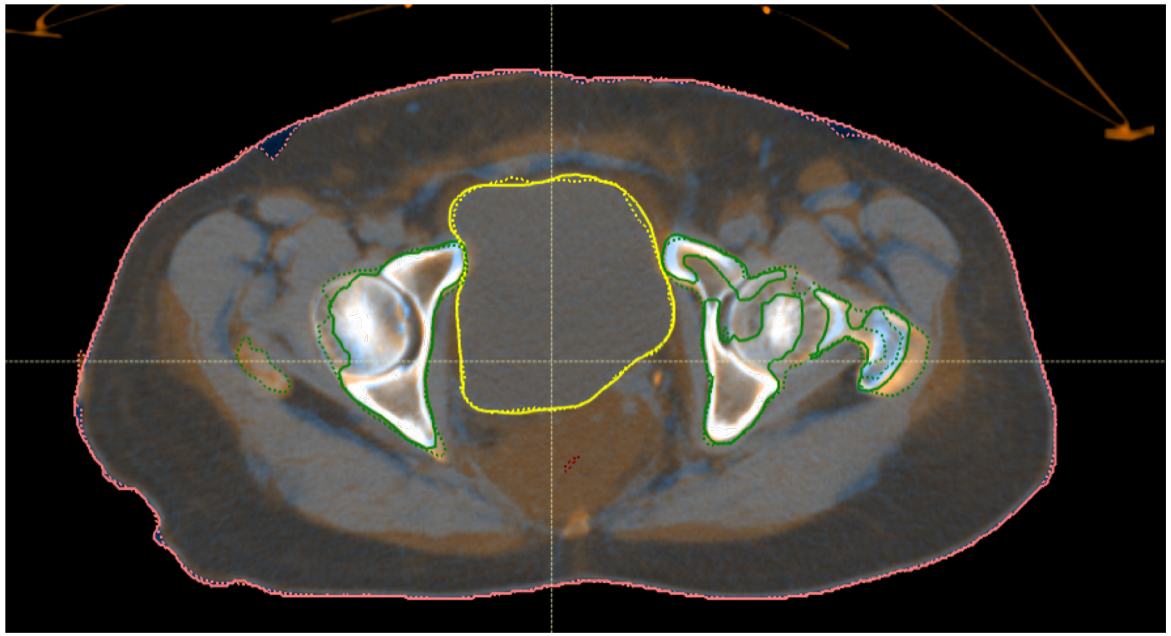
Reirradiation



Supine

DEFORMABLE IMAGE REGISTRATION CAN BE IMPRESSIVE

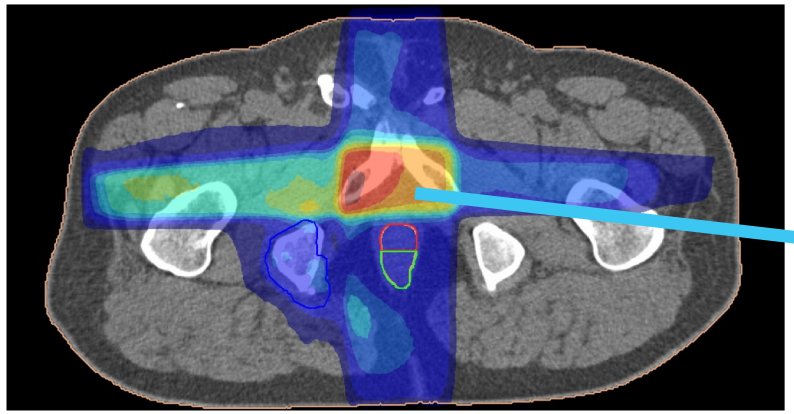




Senthi et al. Comparing rigid and deformable dose registration for high dose thoracic re-irradiation. Radiother Oncol. 2013
Saeed et al. Optimizing Options for Re-irradiation With Deformable Image Registration of Prior Plans. Pract Radiat Oncol. 2013
Lee et al. Re-Irradiation of Hepatocellular Carcinoma: Clinical Applicability of Deformable Image Registration. Yonsei Med J. 2016
Jumeau et al. Optimization of re-irradiation using deformable registration: a case study. *BJR Case Rep*. 2016
Boman et atl. Importance of deformable image registration and biological dose summation in planning of radiotherapy retreatments. Med Dosim. 2017

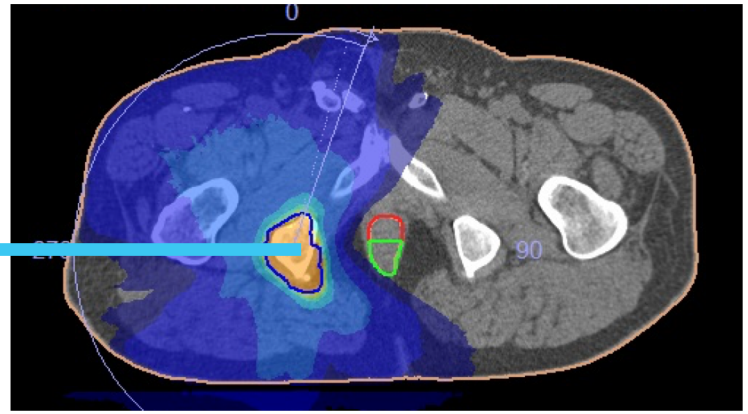
FRACTION-SIZE EFFECTS AND OAR DOSES

Previous (two-phase) 66 Gy / 33 fractions



$EQD2_{\alpha/\beta=3Gy}$
= 120Gy

Reirradiation 30 Gy / 5 fractions

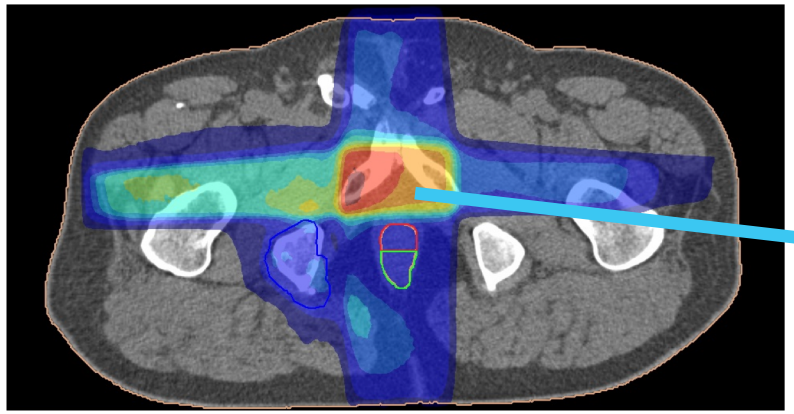


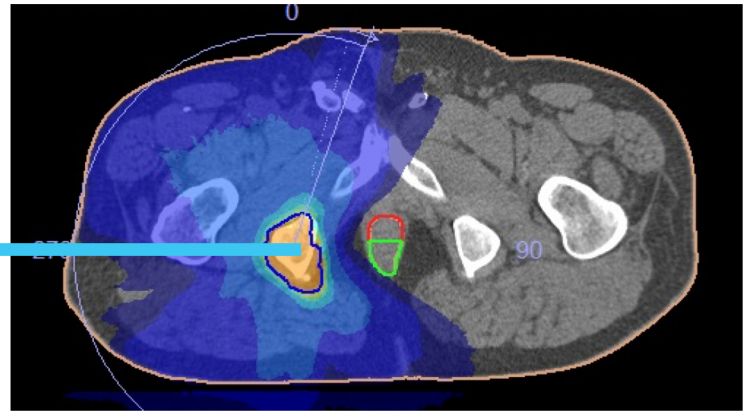
"When an organ or tissue received a significant dose from the initial radiation course, a BED tolerance remaining calculation should be made and an equivalent tolerance in 5 fractions determined" (CtE guidance)

FRACTION-SIZE EFFECTS AND OAR DOSES

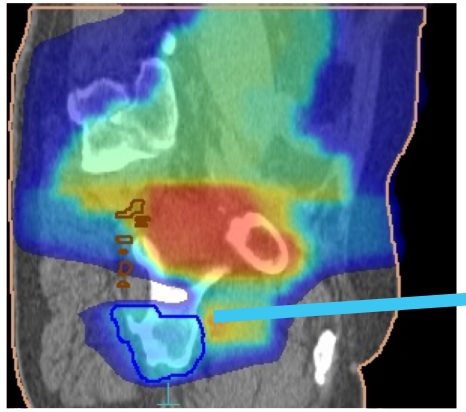
Previous (two-phase) 66 Gy / 33 fractions

Reirradiation 30 Gy / 5 fractions

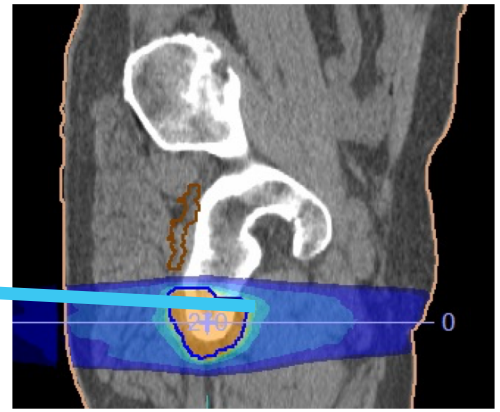




$EQD2_{\alpha/\beta=3Gy}$
= 120Gy



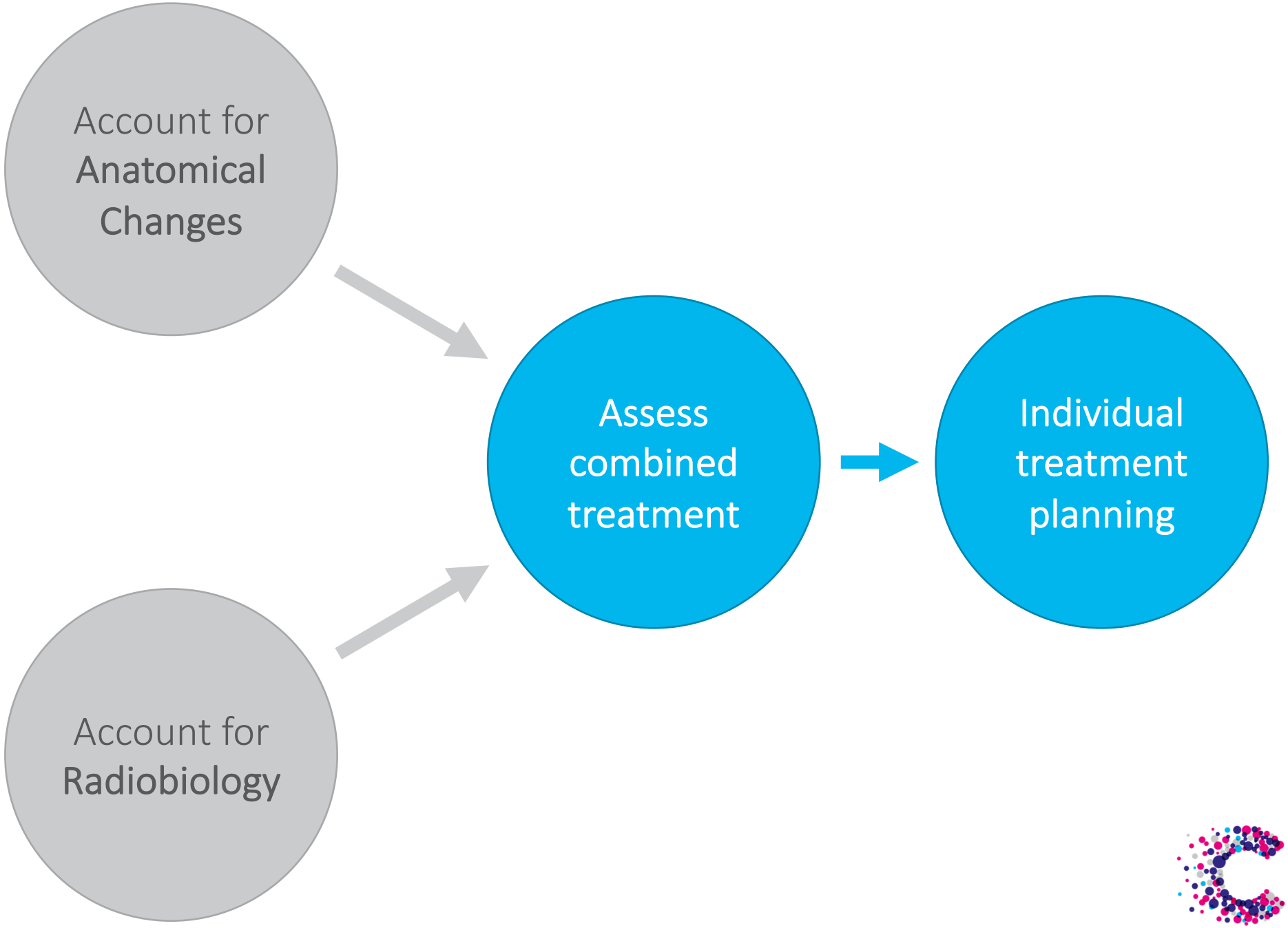
???



Need voxel-by-voxel correction for fraction-size effects!

STRIDeR

Support Tool for Re-Irradiation Decisions guided by Radiobiology

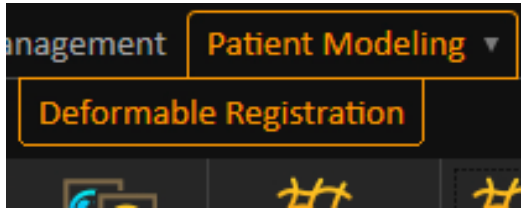


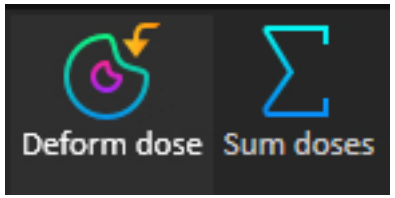
CANCER RESEARCH UK | RADNET LEEDS

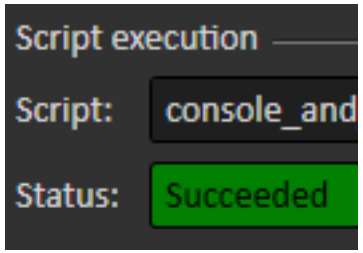
ADVANCED TOOLS AVAILABLE IN MODERN CLINICAL TPS

RayStation

- Deformable Image Registration (DIR)
- Map, sum dose
- Optimise on background dose
- Scripting (Python)
  - ROI, DIR, Dose cubes, Dose statistics, Optimisation functions

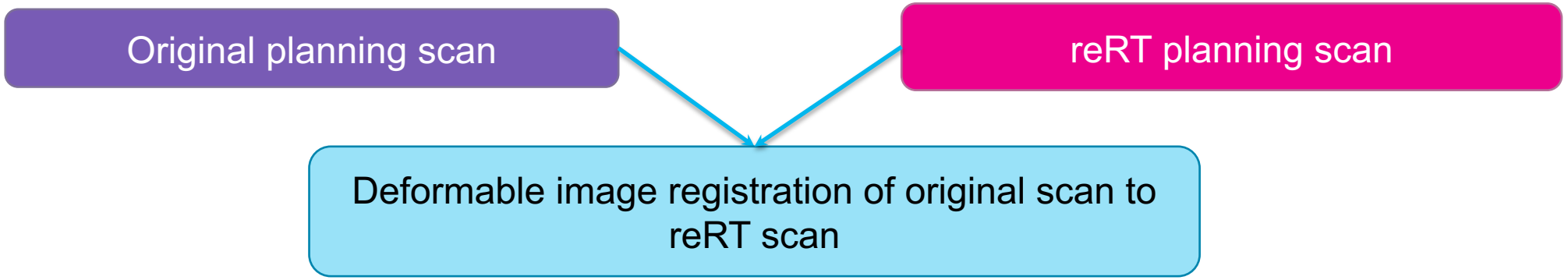






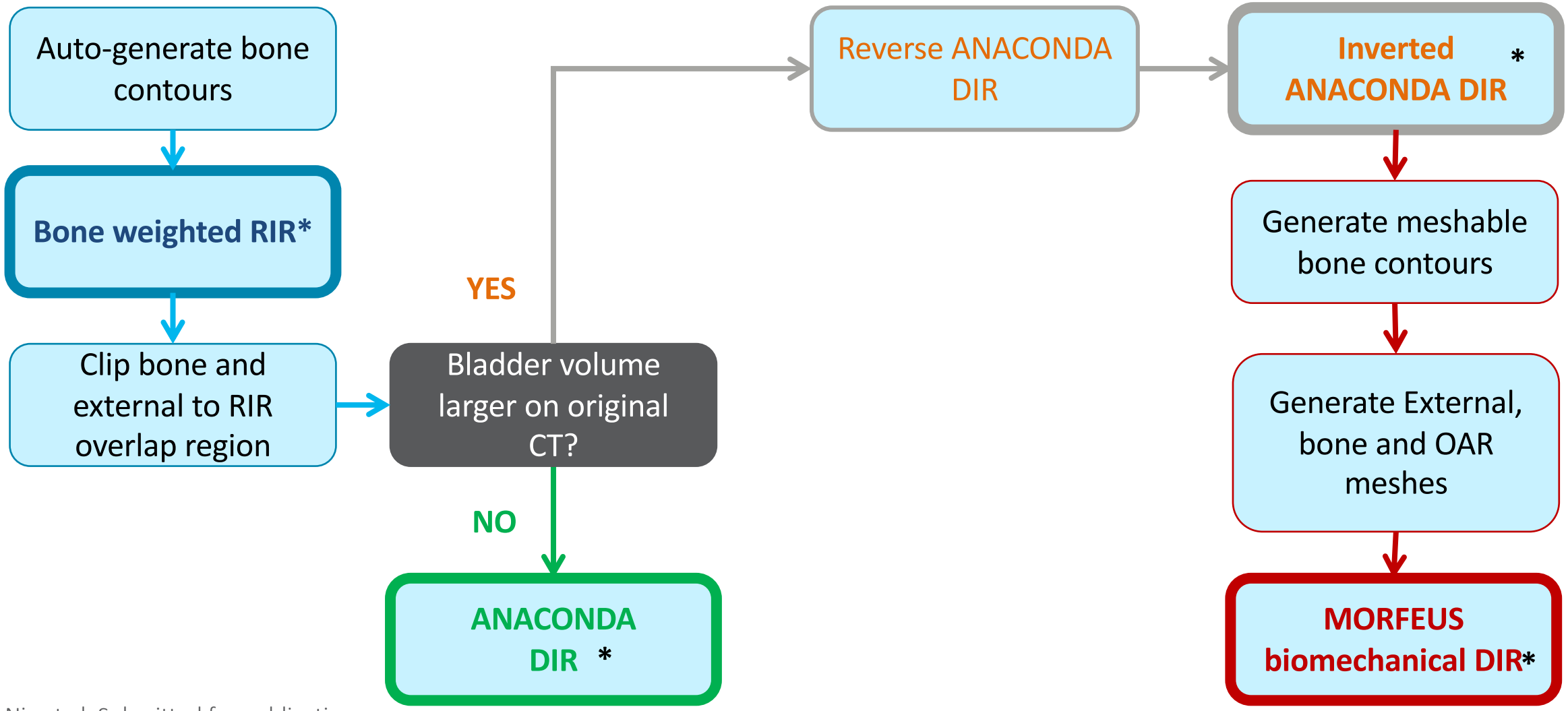
*Custom research build 9B(DTK) *v8.99.110.116*

COMBINED PLAN EVALUATION



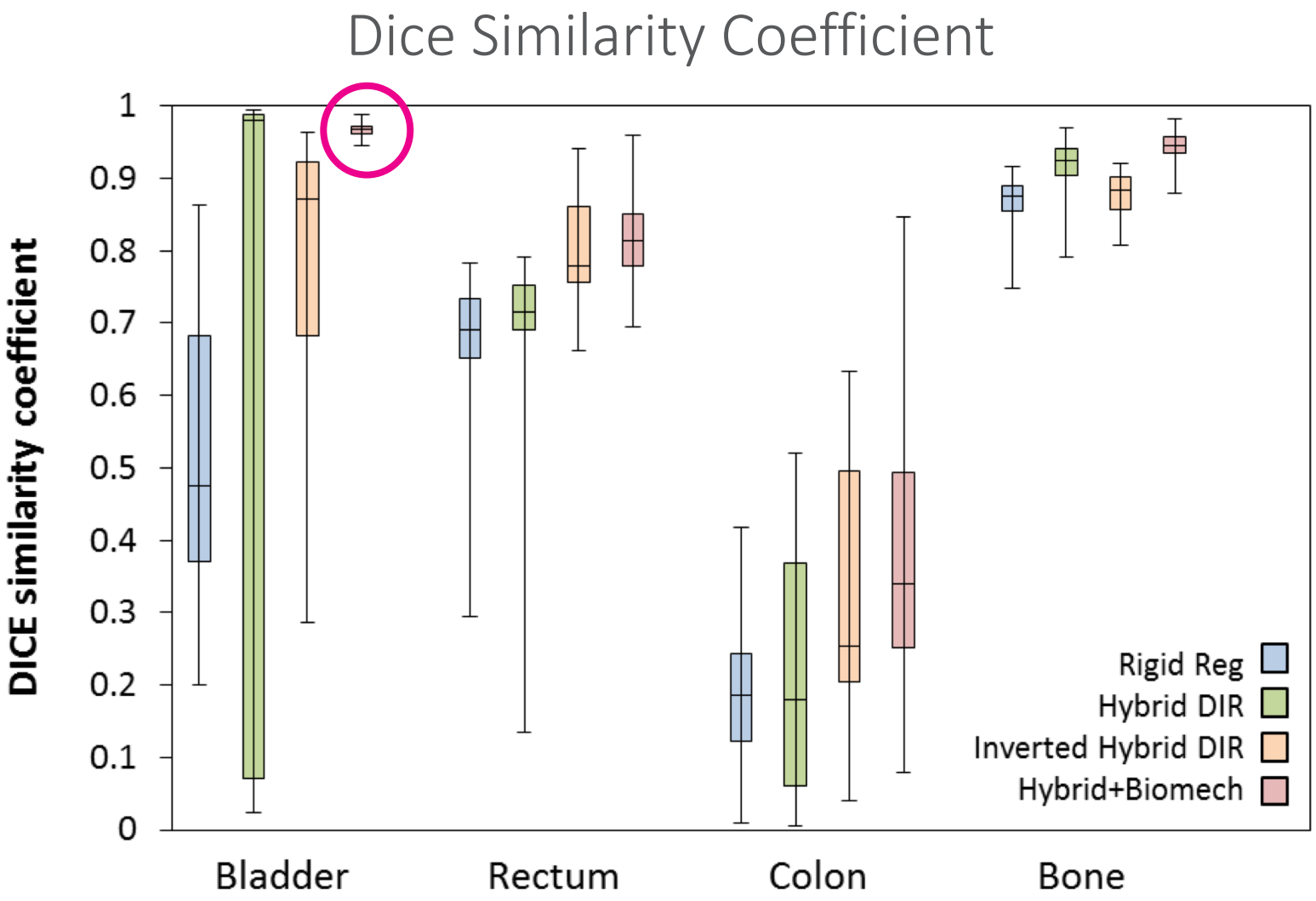
OPTIMISED DIR PROCESS HANDLING EXTREME DEFORMATIONS

(Fully scripted)



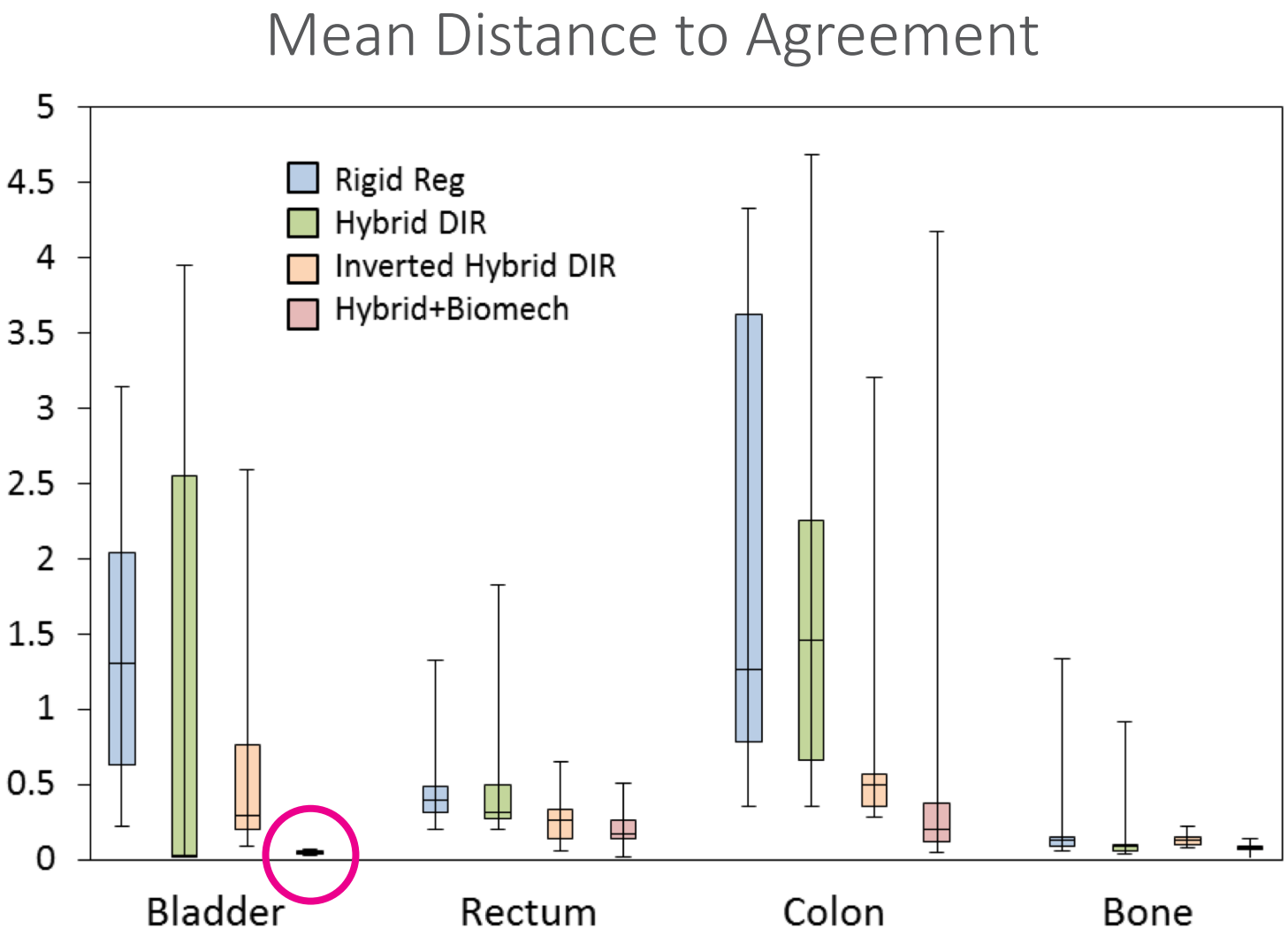
M Nix et al. Submitted for publication

OPTIMISED DIR PROCESS HANDLING EXTREME DEFORMATIONS

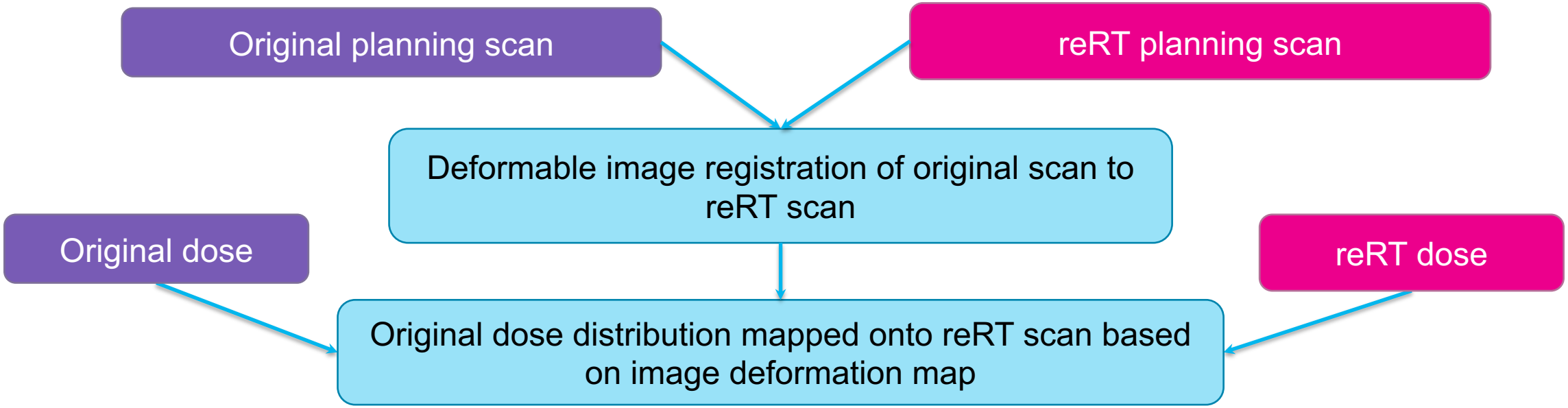


M Nix et al. Submitted for publication

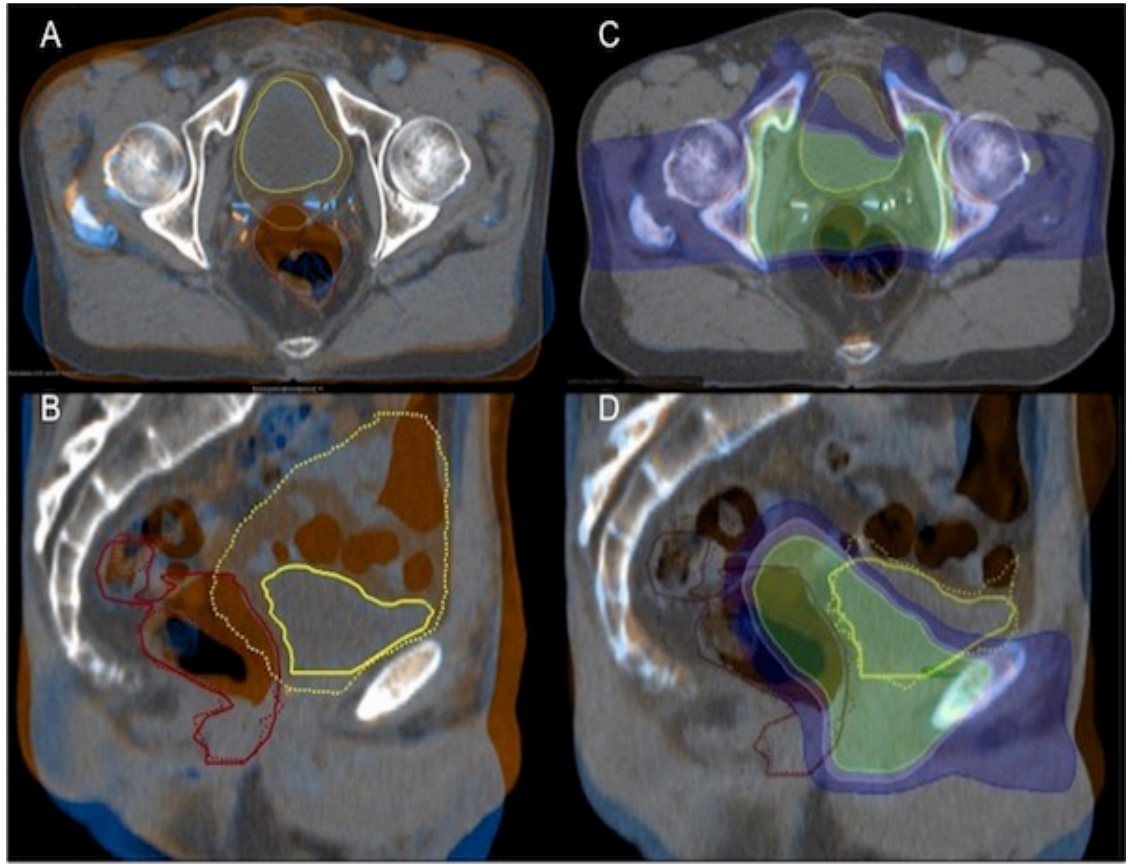
OPTIMISED DIR PROCESS HANDLING EXTREME DEFORMATIONS



COMBINED PLAN EVALUATION

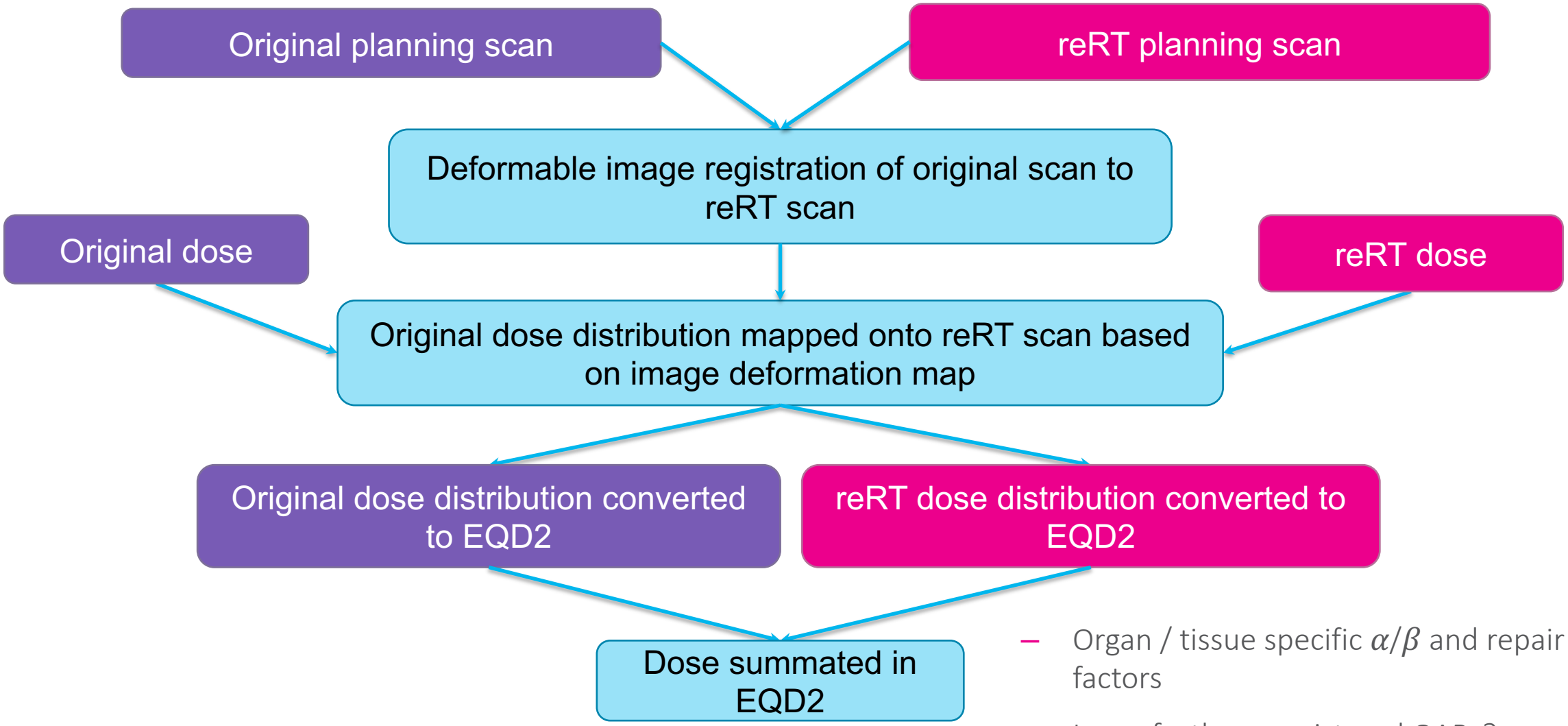


DEFORMABLE IMAGE REGISTRATION WITH DOSE MAPPING



Registrations assessed by two clinicians:
All DIR images of greater clinical relevance than rigidly registered images

COMBINED PLAN EVALUATION



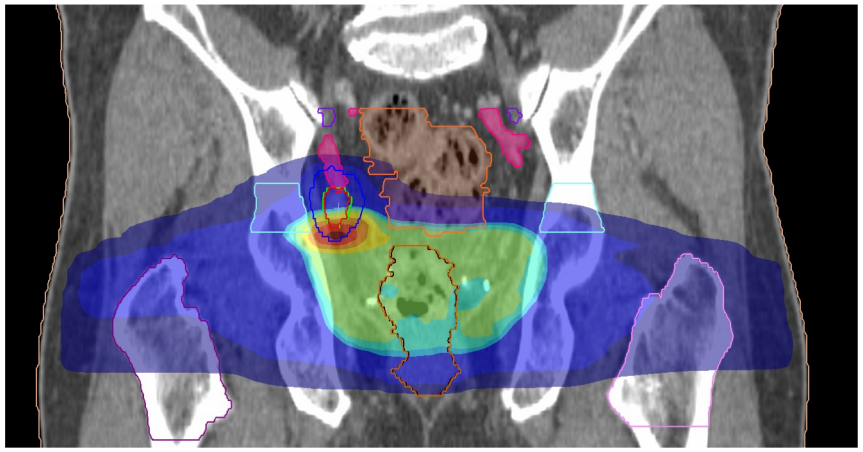
- Organ / tissue specific α/β and repair factors
- Imperfectly co-registered OARs?

EQD2 DOSE SUMMATION

PLAN ASSESSMENT WORKFLOW TEST

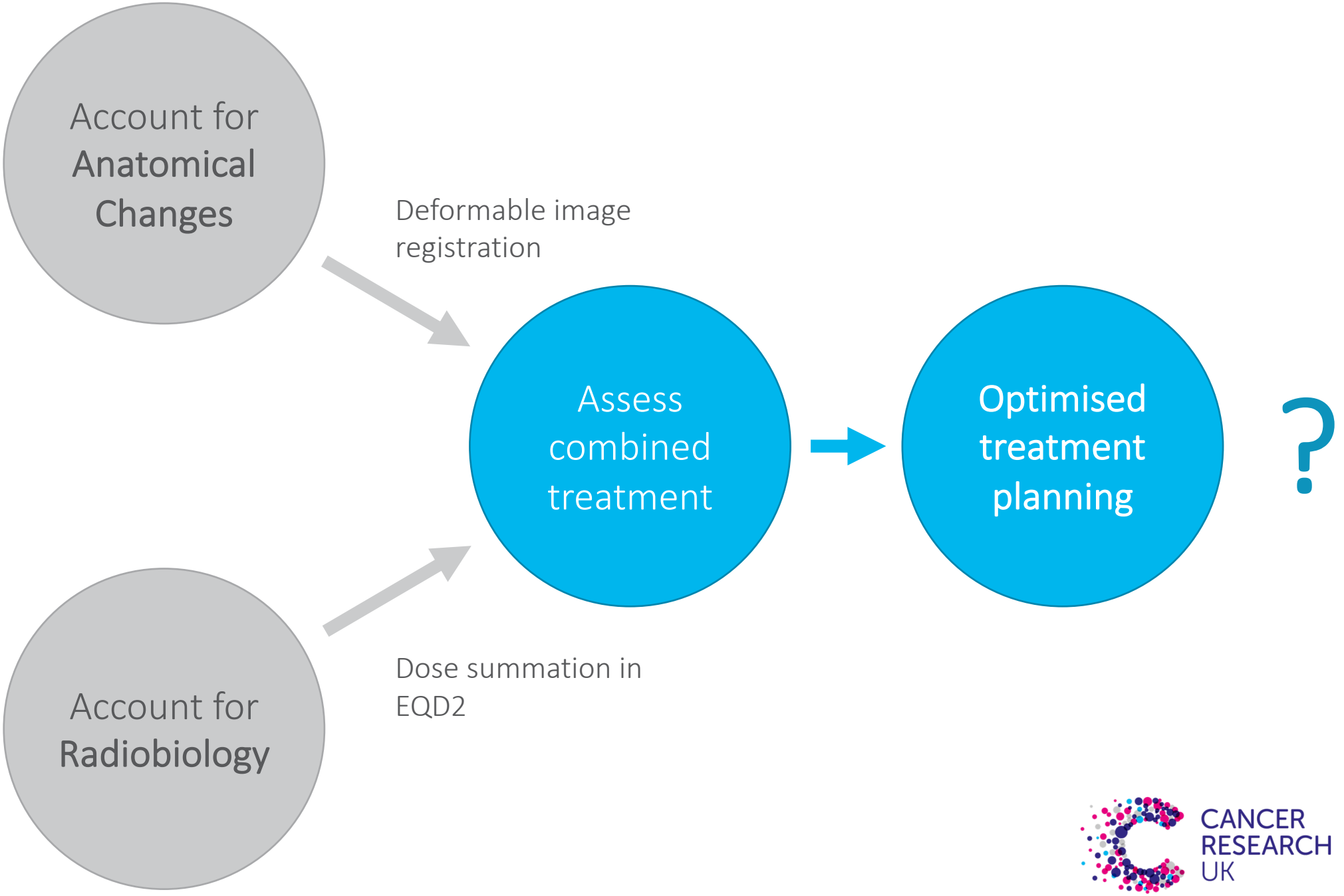
Retrospective cohort of 21 patients

- Previous pelvic radiotherapy 1-9 years prior
- Relapse in region of previously irradiated volume
- Oligometastatic nodal or bone metastases
- 18:3 male:female
- Original CT + dose; reRT CT + dose



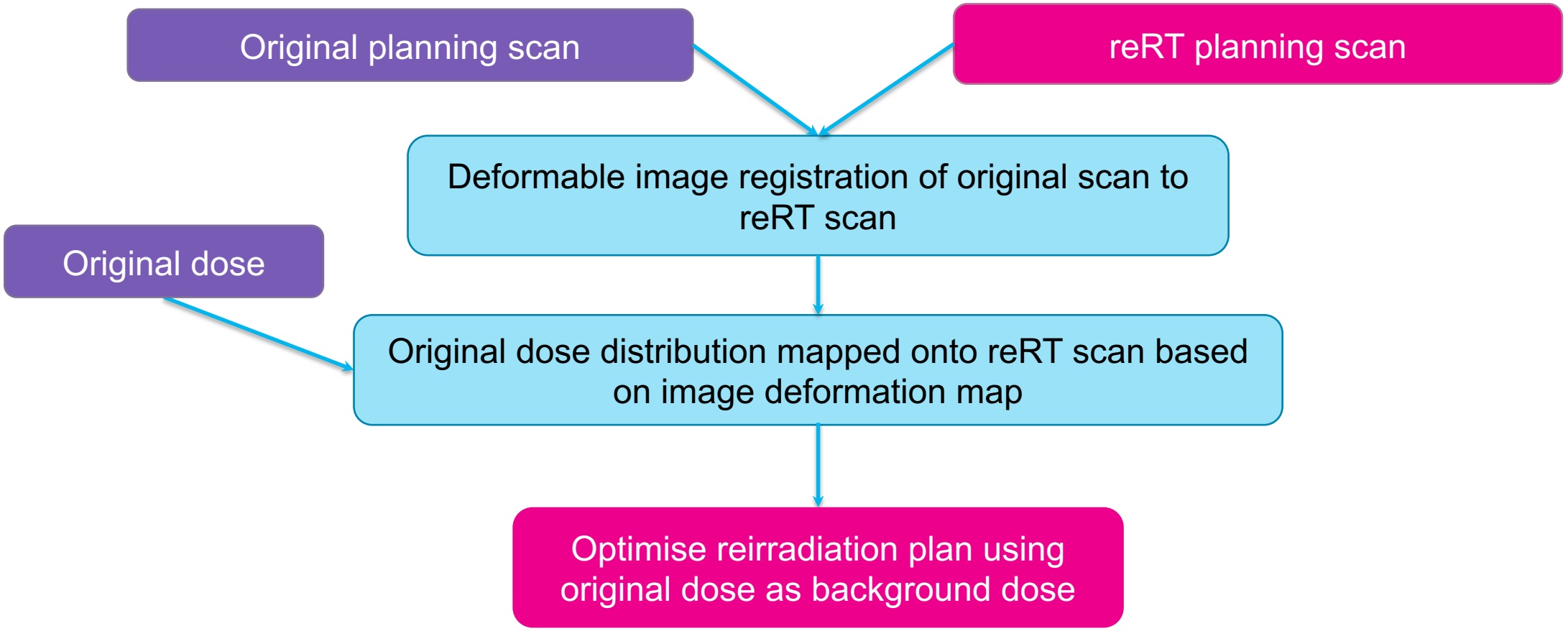
11/21 patients had at least one OAR dose change >20% using DIR rather than RIR

3/21 patients had at least one OAR max dose >90Gy EQD2



CANCER RESEARCH UK | RADNET LEEDS

OPTIMISATION OF REIRRADIATION



PLANS MUST BE OPTIMISED IN EQD2 (BED)

- Cumulative dose constraints for OARs for reirradiation (or multi-phase) treatments are only well-defined in EQD2 (BED)
- Plan optimization taking background dose into account must happen in EQD2 (BED) space
- Not currently available in clinical TPS

Implemented in RayStation

OPTIMISING PLANS IN EQD2

Workflow

- Register original CT to reRT CT with DIR
- Deform original dose to reRT CT
- Set original dose as background dose
- Plan reRT as normal (fractions, dose prescription, etc)
  - OAR objectives: Define and optimise in EQD2 on combined doses
  - Target objectives: Define and optimise as physical objectives for reRT plan only
- Assess new plan in physical dose (conformality, etc)
- Assess combined plans in EQD2

EQD2 OPTIMISATION IN RAYSTATION (WORK IN PROGRESS!)

Target objectives in physical dose, reRT plan only

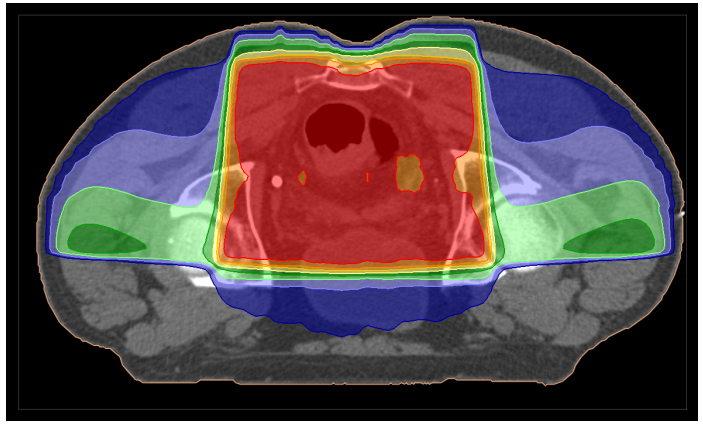
Additional conformality (in EQD2) taking original dose into account

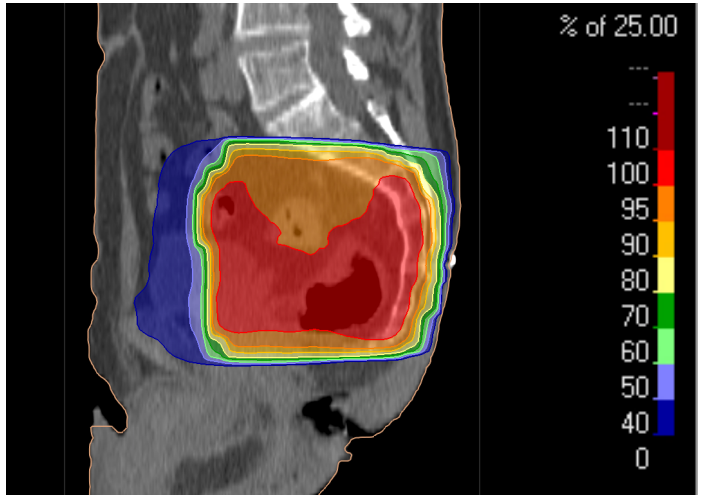
OAR objectives for combined doses in EQD2

Organ specific α/β and repair

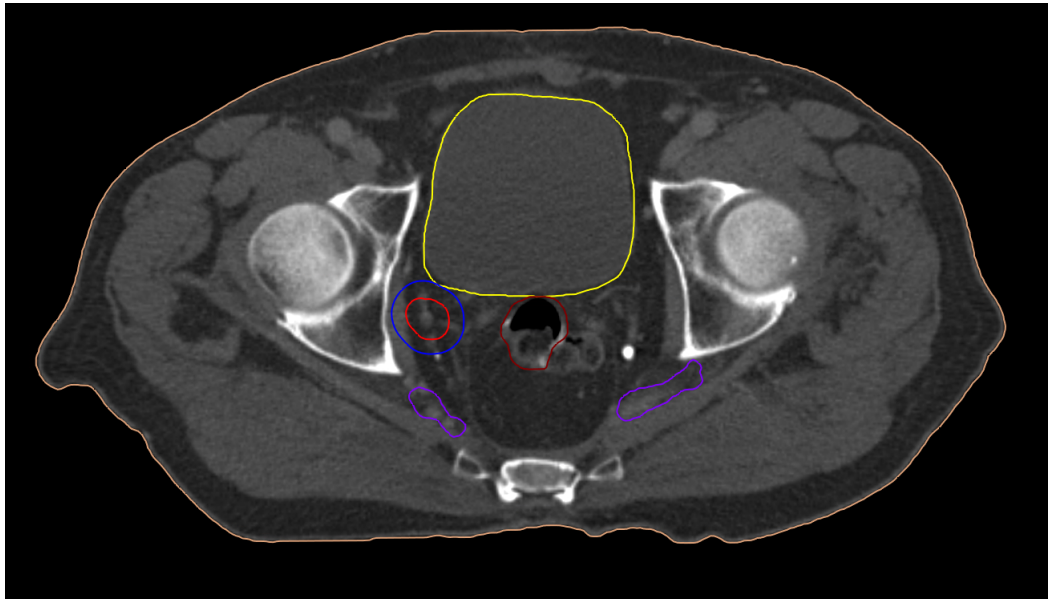
EQD2 OPTIMISATION IN RAYSTATION (WORK IN PROGRESS!)

Original treatment:
25 Gy / 5 fractions





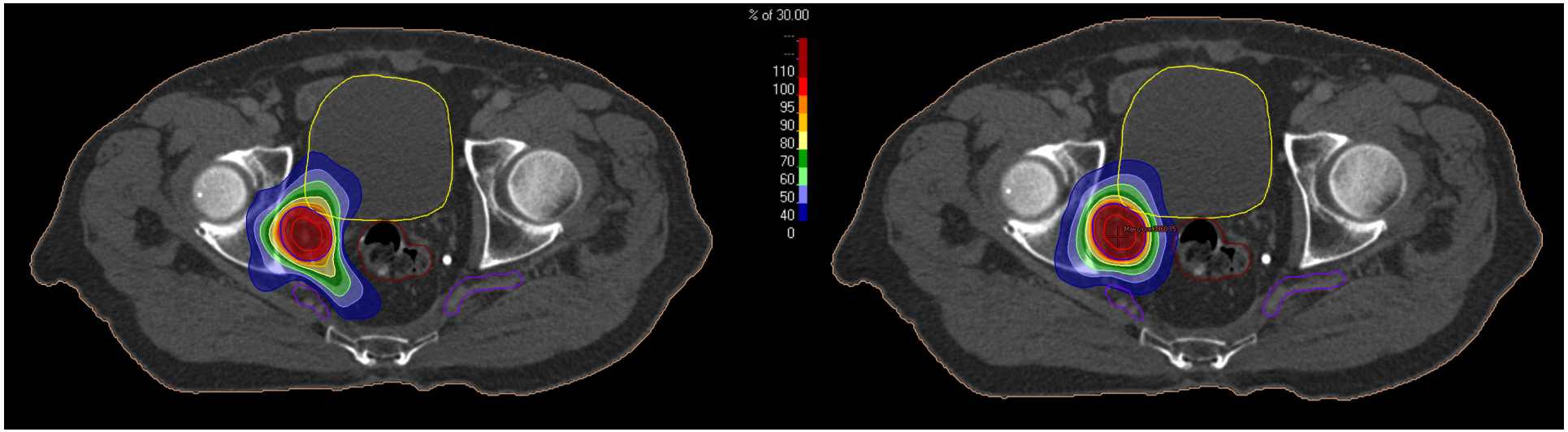
Nodal recurrence:
30 Gy / 5 fractions SABR

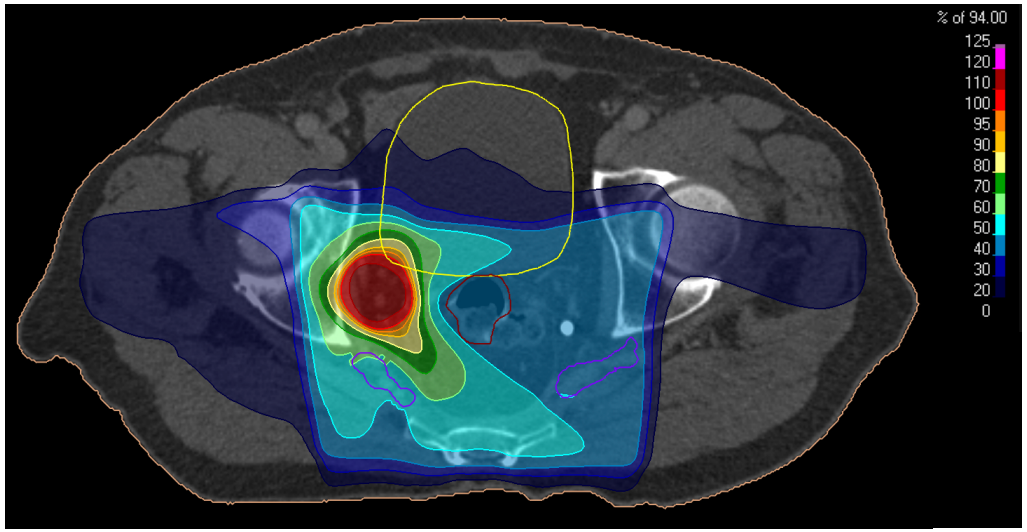


EQD2 OPTIMISATION IN RAYSTATION (WORK IN PROGRESS!)

Optimised using combined EQD2

Optimised using combined physical

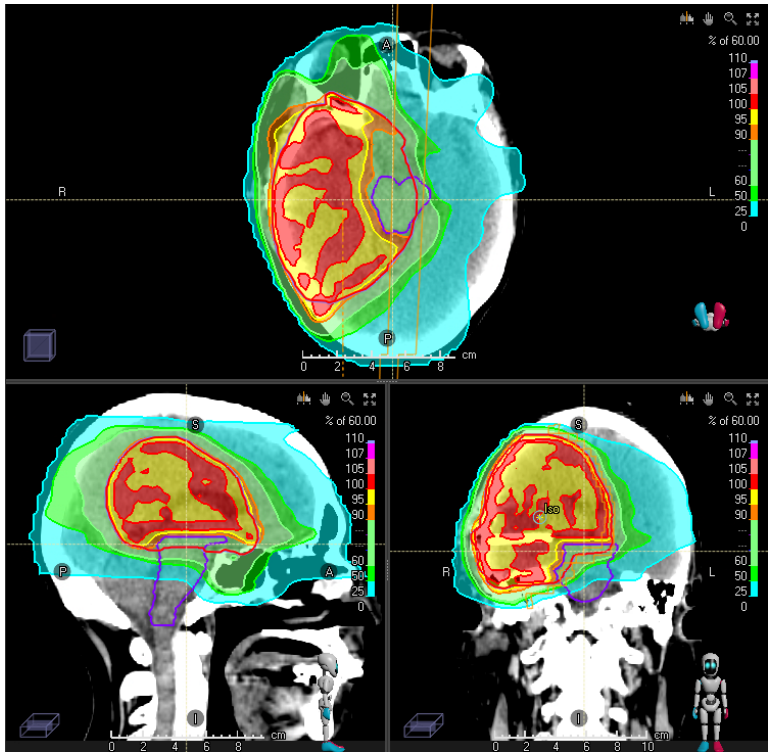




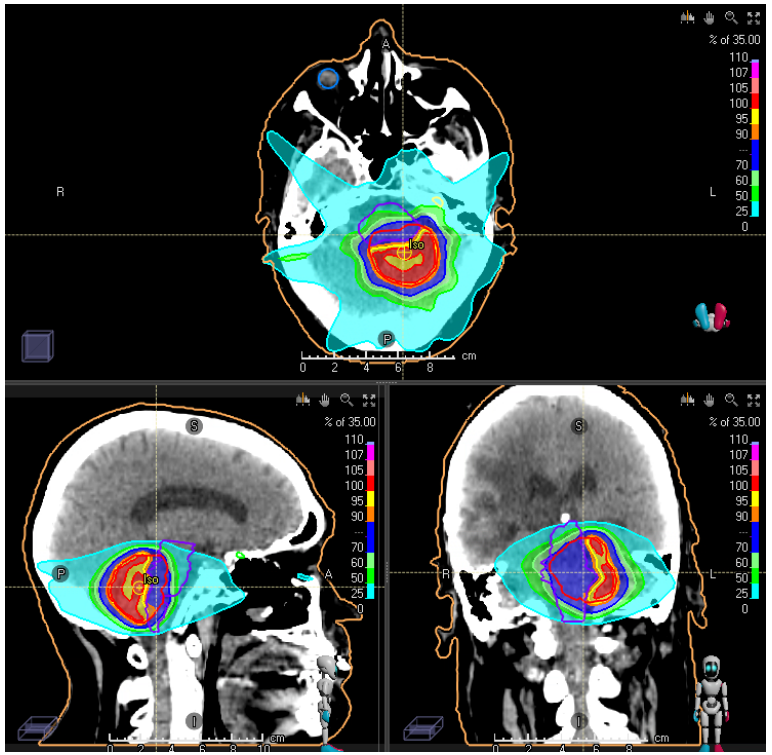
Combined doses in EQD2

EQD2 OPTIMISATION IN RAYSTATION (WORK IN PROGRESS!)

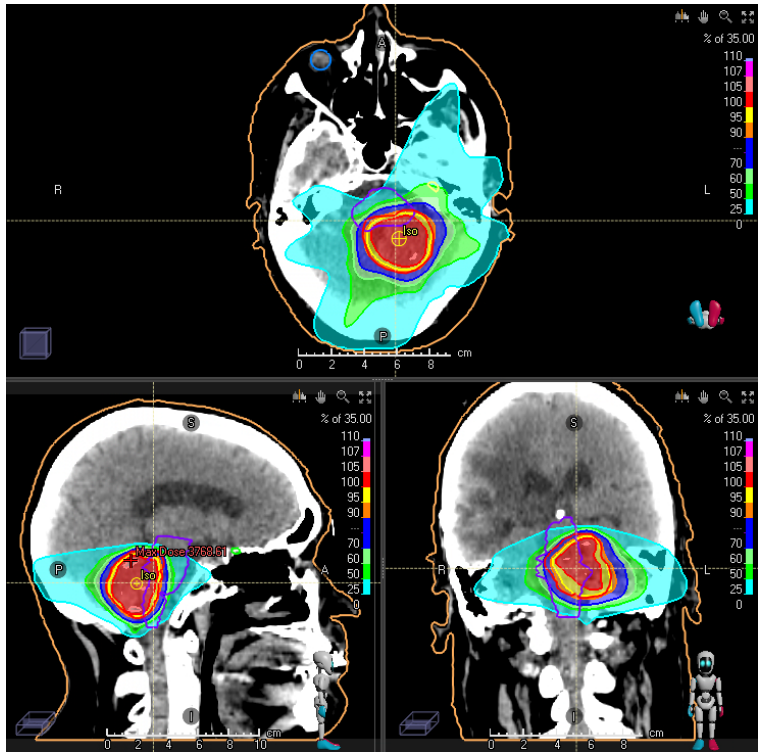
Initial treatment



Optimised using previous brainstem D_{max} to determine OAR constraint



Optimised using combined EQD2



Example curtesy of Jonathan Entwisle

NEXT STEPS & FUTURE PERSPECTIVES

Analyse existing CtE data

Use for patient treatments

- Feasibility study
- Clinical trial – can we considerably individualise treatment and/or the number of patients offered re-irradiation?

More tumour sites

Functional imaging, adaptive treatment, modelling-based plan individualisation, …

SUMMARY & TAKE HOME MESSAGES

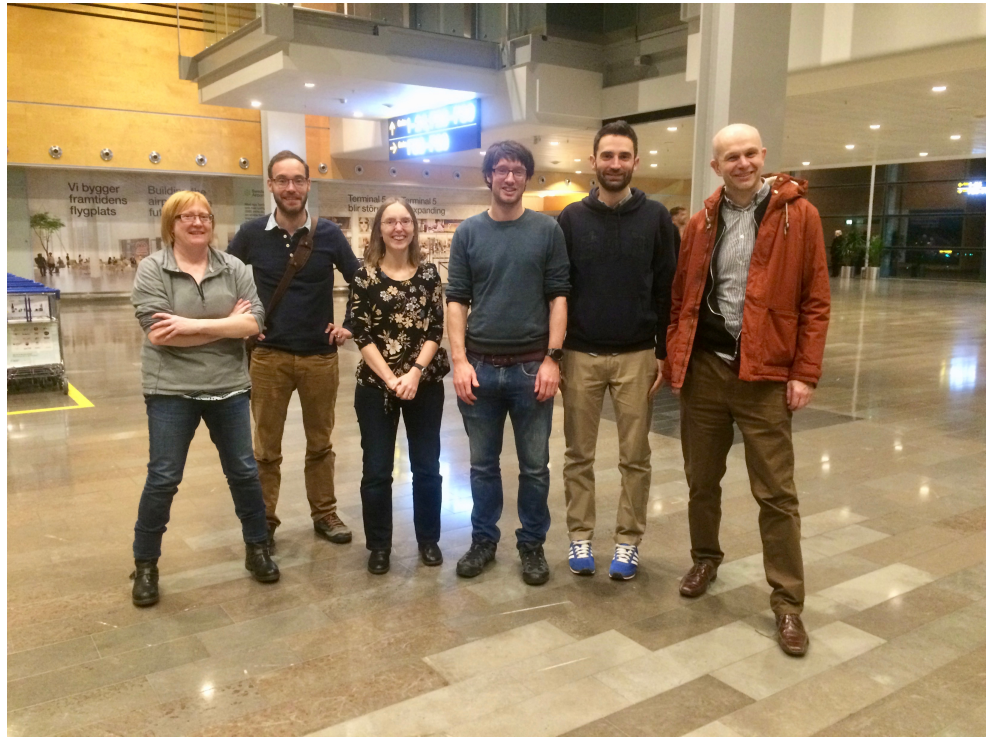
National evaluation programmes can help generate evidence & high quality data in reirradiation

Significant technical challenges in re-irradiation planning & delivery

- Accounting for both anatomical changes & fraction-size effects essential
- We have the tools, but we have not routinely implemented them for reRT

Reirradiation: wide open for research and innovation

THE STRIDeR TEAM



Louise Murray
John Lilley
Steven Gregory
Mike Nix
Mike Aldred
Lynn Aspin

Stina Svensson
Ola Weistrand
Julien Uzan
Kjell Eriksson

RaySearch Laboratories

yorkshire cancer research

The Leeds Teaching Hospitals NHS
NHS Trust

UNIVERSITY OF LEEDS

CANCER RESEARCH UK

RADNET LEEDS

AAPM COMP 2020

THANK YOU

Ane Appelt

Associate Professor, University of Leeds, UK

@cancerphysicist