UK Approaches to Rel Irradiation
SABR reirradiation with DIR and EQD2 optimisation

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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

Lack of standard treatment

Heterogeneous poor quality data
EVIDENCE CHALLENGE IN REIRRADIATION

Clinical trials

Standardized treatment

Better quality data

Clinical guidelines

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

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CtE

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

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

Reirradiation

Prone

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
Boman et al. Importance of deformable image registration and biological dose summation in planning of radiotherapy retreatments. Med Dosim. 2017
FRACTION-SIZE EFFECTS AND OAR DOSES

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

\[ \text{EQD}_{2\alpha/\beta=3\text{Gy}} = 120\text{Gy} \]

Need voxel-by-voxel correction for fraction-size effects!
STRIDeR
Support Tool for Re-Irradiation Decisions guided by Radiobiology
Account for Anatomical Changes

Account for Radiobiology

Assess combined treatment

Individual treatment planning
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

Original planning scan

Deformable image registration of original scan to reRT scan

reRT planning scan
OPTIMISED DIR PROCESS HANDLING EXTREME DEFORMATIONS
(Fully scripted)

Auto-generate bone contours

Bone weighted RIR*

Clip bone and external to RIR overlap region

Bladder volume larger on original CT?

YES

Reverse ANACONDA DIR

Inverted ANACONDA DIR*

Generate meshable bone contours

Generate External, bone and OAR meshes

NO

ANAConDA DIR *

MORFEUS biomechanical DIR*
OPTIMISED DIR PROCESS HANDLING EXTREME DEFORMATIONS

Dice Similarity Coefficient

[Graph showing Dice Similarity Coefficient for various anatomical structures (Bladder, Rectum, Colon, Bone) with different registration methods (Rigid Reg, Hybrid DIR, Inverted Hybrid DIR, Hybrid+Biomech).]

M Nix et al. Submitted for publication
OPTIMISED DIR PROCESS HANDLING EXTREME DEFORMATIONS

Mean Distance to Agreement

- Rigid Reg
- Hybrid DIR
- Inverted Hybrid DIR
- Hybrid+Biomech

Bladder
Rectum
Colon
Bone
COMBINED PLAN EVALUATION

Original planning scan → Deformable image registration of original scan to reRT scan → Original dose distribution mapped onto reRT scan based on image deformation map → reRT dose

Original dose

reRT planning scan
Registrations assessed by two clinicians:
All DIR images of greater clinical relevance than rigidly registered images
Original planning scan ➔ Deformable image registration of original scan to reRT scan ➔ Original dose distribution mapped onto reRT scan based on image deformation map ➔ Original dose distribution converted to EQD2 ➔ reRT dose distribution converted to EQD2 ➔ Dose summated in EQD2

- Organ / tissue specific $\alpha/\beta$ 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
Account for Anatomical Changes

Account for Radiobiology

Deformable image registration

Assess combined treatment

Dose summation in EQD2

Optimised treatment planning

?
OPTIMISATION OF REIRRADIATION

Original planning scan

Deformable image registration of original scan to reRT scan

Original dose distribution mapped onto reRT scan based on image deformation map

Optimise reirradiation plan using original dose as background dose
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 conformity (in EQD2) taking original dose into account

OAR objectives for combined doses in EQD2

Organ specific $\alpha/\beta$ 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 $D_{\text{max}}$ to determine OAR constraint

Optimised using combined EQD2

Example courtesy 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

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THANK YOU

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