Treatment delivery uncertainties in rectal cancer radiotherapy – evidence-based margin estimates

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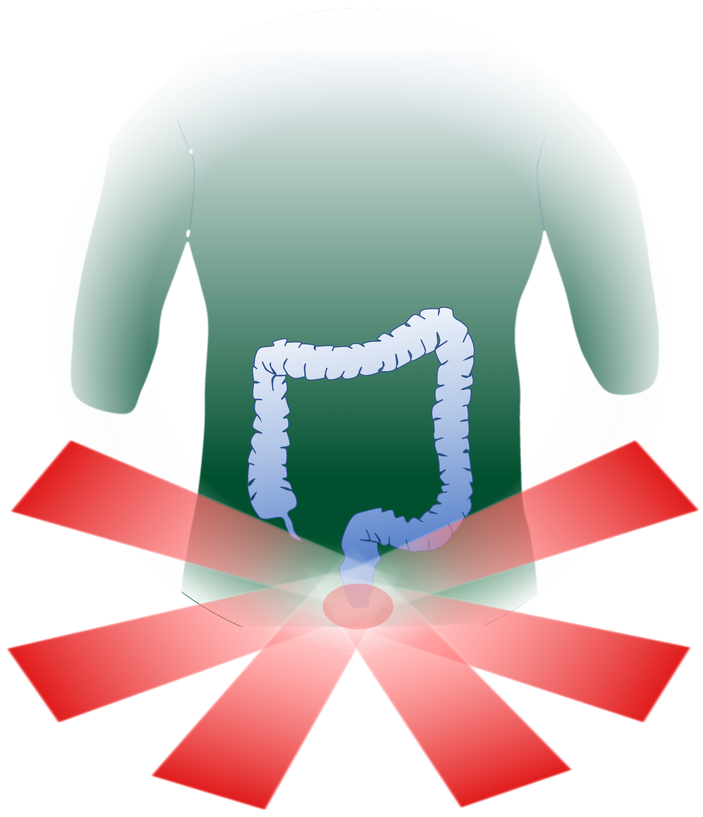
Background & Objective

- Multiple studies have evaluated individual sources of uncertainty associated with rectal cancer radiotherapy delivery
- Only limited practical guidance has been available to guide local centre-specific choice of treatment margins

We reviewed the literature, and combined relevant data to estimate PTV margins for long-course chemoradiotherapy (LCRT) for various image guidance strategies.



Conclusions

- PTV margins can be estimated for rectal cancer LCRT based on available published evidence.
- **An interactive app, available at http://tiny.cc/5qsqez, provides PTV margins for different scenarios,** including variable values for delineation and setup uncertainty.
- This work can form the basis for IMRT guidelines, with the addition of clinical expertise and consensus.

Results

- Relevant sources of treatment delivery uncertainty, as well as data for systematic (Σ) and random (σ) uncertainties, are summarised in lower right table.
- Multiplicative factors for systematic uncertainties (corresponding to α in the van Herk formula) were set to 2.51 (for GTV) and 2.58 (for CTV, see Nijkamp at al 2012, taking deformations into account).
- The corresponding factor for random uncertainties (β) was set to 1.28.
- Penumbra (σ_{pen}) in soft tissue was assumed to be 3mm.
- Insufficient data were available to estimate cranio-caudal margins for the CTV.

Table 2 summarises appropriate margins for daily imaging and setup on bony anatomy.

A no-action-level (NAL) strategy, with 3 initial daily images plus weekly imaging, resulted in a 1-2mm increase in margin estimates. Reduced delineation uncertainty decreased margins, but increased impact of daily versus NAL imaging.

	Anterior	Posterior	Lateral	Medial	Cranio-caudal
GTV	10	10	7	N/A	13
CTV					
Mesorectum upper	18	7	7	N/A	*
Mesorectum lower	12	7	7	N/A	*
Presacral	12	7	7	N/A	*
Lateral nodes	12	7	7	8	
Sphincter	8	12	8	N/A	*

Example margins [in mm] for LCRT with daily imaging, assuming $\Sigma_{delineation}$ = 1mm.
* No data available

Material & methods

- Sources of uncertainty in rectal cancer radiotherapy delivery identified through literature review.
- Sources of uncertainty divided into systematic and random uncertainties, as per ICRU 83.
- Some uncertainties and treatment details were considered general for (pelvic) radiotherapy, and were sourced from the general radiotherapy literature. They included
  - mechanical factors for the treatment delivery platform
  - variation in image match on bony structures
  - residual uncorrected rotation
- Others uncertainties were specific to rectal cancer radiotherapy, for example
  - interobserver delineation variation
  - inter-/intrafraction soft tissue shifts relative to bony structures
- All factors were evaluated separately for the primary tumour (GTV) and the elective nodal volumes (CTV), with different nodal compartments of the CTV evaluated separately.
- Margins were calculated with the intention of delivering 90% of the planned dose to the treatment targets for 90% of patients, as appropriate for neoadjuvant treatment.
- Margins were calculated using the van Herk approach (van Herk et al, 2000):

$$\alpha\sqrt{\Sigma_1^2+\Sigma_2^2+\cdots+\Sigma_n^2}+\beta\left(\sqrt{\sigma_1^2+\sigma_2^2+\cdots+\sigma_n^2+\sigma_p^2}-\sigma_p^2\right)$$

	Primary tumour	Elective volumes	Source / notes
Systematic errors Σ [mm]			
Delineation	1	1	Significant variation in the literature; centre dependent; see e.g. Nijkamp 2012, Burbach 2016, Franco 2018. This value valid for MRI-based delineation.
Mechanical	0.5	0.5	Difference in kV & MV isocentre, mechanical lash/play, etc
Soft tissue shift / deformation	2.3 - 4.8	1.5 - 5.5	Relative to bony structures; direction dependent; varies for different nodal compartments. See primary publications for details (Kleijnen 2019 for GTV; Nijkamp 2012 for CTV).
Setup (bony structures)			
NAL (no action limit) protocol	1.4	1.4	Example values; valid if correcting mean setup error over treatment course to ±2.5mm.
Daily imaging	N/A	N/A	
Random errors σ [mm]			
Mechanical	1.0	1.0	MLC positioning, match / couch movement uncertainties, etc
Uncorrected rotation	0.5	0.5	Based on Laursen 2012; assuming 5-7cm GTV and 20cm CTV, with match centred on GTV / CTV.
Inter- & intra-observer image registration	0.5	0.5	Based on data for automatic matching of bony structures for pelvic phantom (Barber 2016)
Intrafraction movement	1.5	2.3	Based on Kleijnen 2016; assuming ~10min on couch
Soft tissue shift / deformation	1.5 - 3.3	1.5 - 4.0	Relative to bony structures; direction dependent; varies for different nodal compartments. See primary publications for details (Kleijnen 2019 for GTV; Nijkamp 2012 for CTV).
Setup (bony structures)			
NAL (no action limit) protocol	2.5	2.5	Example values, highly dependent on local setup procedures. See Hurkmans 2001.
Daily imaging	N/A	N/A	

References

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Acknowledgement

Partly funded by Yorkshire Cancer Research through a University Academic Fellowship for Ane Appelt (L389AA)

yorkshire cancer research

ESTRO2020 PO-1638

Physics track: Adaptive radiotherapy and inter-fraction motion management

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DOI: 10.3252/pso.eu.ESTRO2020.2020

Poster presented at: ESTRO

PosterSessionOnline.com