UMC Utrecht
Cancer Center

Session 3 - Optimizing Results

Boost by External Beam Radiotherapy

Martijn Intven – Radiation Oncologist

Boost by External Beam Radiotherapy

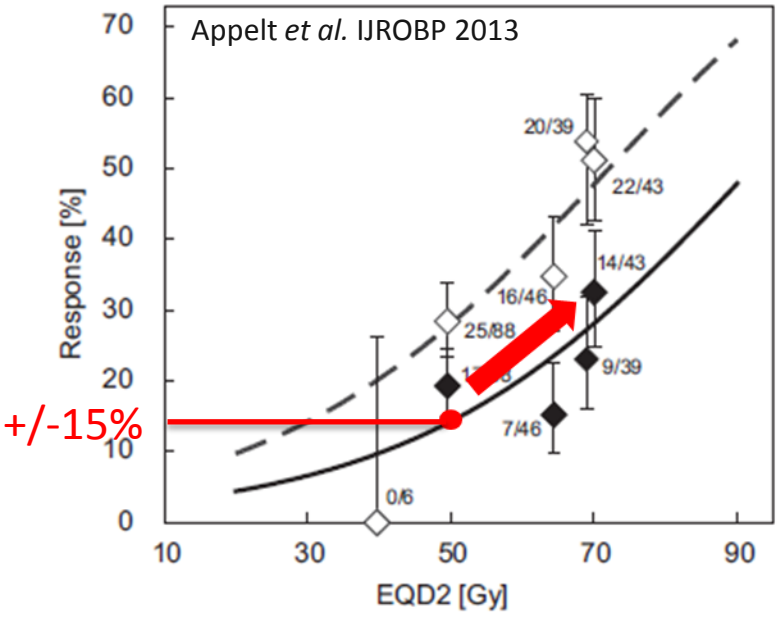
Dose-effect relationship:

- Standard of care in locally advanced rectal cancer:
  - 45-50.4 Gy in 25/28 fractions + 5-FU based chemotherapy and TME surgery 8-12 weeks later

→ Approximately 15% pCR

- Dose escalation

→ ?? pCR



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1. Sanghera et al, *Clin Oncol 2008; 20(2):176-83*
2. Maas et al, *Lancet Oncol 2010; 11: 835–44*

Boost by External Beam Radiotherapy

Dose-effect relationship:

- Meta-analysis > 60 Gy:

Contents lists available at ScienceDirect

Radiotherapy and Oncology

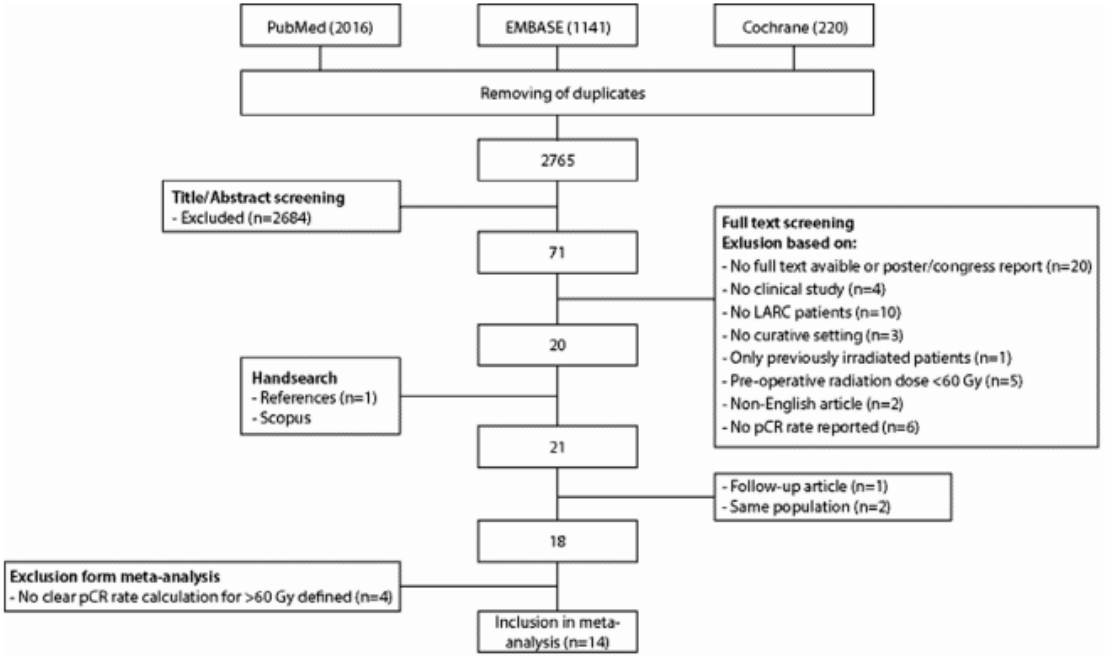
journal homepage: www.thegreenjournal.com

Systematic review

Impact of radiotherapy boost on pathological complete response in patients with locally advanced rectal cancer: A systematic review and meta-analysis

Johannes Peter Maarten Burbach [a,*,1], Annemarie Maria den Harder [b,1], Martijn Intven [a], Marco van Vulpen [a], Helena Marieke Verkooijen [c], Onne Reerink [a]

[a] Department of Radiation Oncology; [b] Department of Radiology; and [c] Trial Bureau Imaging Division, University Medical Center, Utrecht, The Netherlands



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Burbach et al, *Radioth. & Oncol. 2014; 113:1-9*

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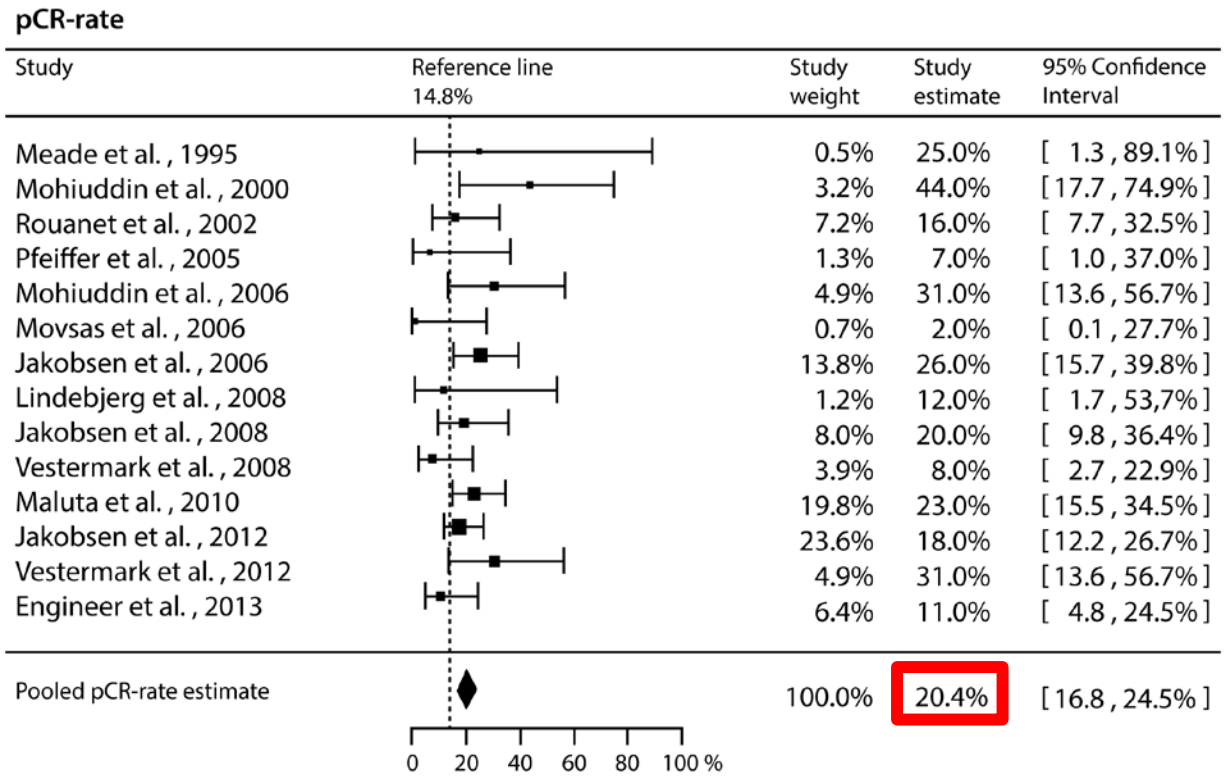

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Acute grade 3-4 toxicity

Study	Study weight	Study estimate	95% Confidence Interval
Meade et al., 1995	3.5%	25.0%	[1.3, 89.1%]
Mohiuddin et al., 2000	9.4%	33.3%	[11.1, 66.7%]
Pfeiffer et al., 2005	6.5%	7.1%	[1.0, 37.0%]
Mohiuddin et al., 2006	11.6%	43.8%	[22.5, 67.6%]
Movsas et al., 2006	10.2%	14.3%	[4.7, 36.1%]
Jakobsen et al., 2006	10.6%	6.0%	[1.9, 17.0%]
Jakobsen et al., 2008	9.2%	5.7%	[1.4, 20.2%]
Vestermark et al., 2008	9.2%	5.6%	[1.4, 19,7%]
Maluta et al., 2010	6.7%	1.3%	[0.2, 8.80%]
Jakobsen et al., 2012	13.5%	10.1%	[5.7, 17.3%]
Engineer et al., 2013	9.2%	4.5%	[1.1, 16.4%]
Pooled toxicity estimate	100.0%	10.3%	[5.4, 18.6%]

0 20 40 60 80 100%

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Burbach et al, *Radioth. & Oncol. 2014; 113:1-9*

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EBRT boost strategies:

Study	Boost approach	Boost timing
Meade et al. 1995	EBRT	Sequential
Mohiuddin et al. 2000	EBRT	Sequential
Rouanet et al. 2002	EBRT	Sequential
Pfeiffer et al. 2005	EBRT	Integrated (SIB) and Sequential
Jakobsen et al. 2006	Brachytherapy	Sequential
Mohiuddin et al. 2006	EBRT	Integrated (SIB)
Movsas et al. 2006	EBRT	Sequential
Jakobsen et al. 2008	EBRT + Brachytherapy	Sequential
Vestermark et al. 2008	EBRT	Integrated (SIB) and Sequential
Lindebjerg et al. 2009	EBRT + Brachytherapy	Integrated (SIB) and Sequential
Maluta et al. 2010	EBRT	Sequential
Jakobsen et al. 2012	Brachytherapy	Sequential
Vestermark et al. 2012	Brachytherapy	Integrated (SIB) and Sequential
Engineer et al. 2013	EBRT	Sequential

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Burbach et al, *Radioth. & Oncol. 2014; 113:1-9*

Boost by External Beam Radiotherapy

EBRT boost strategies:

- Integrated (SIB = simultaneous integrated boost)

- Sequential
  - Start with boost

  - End with boost

- Combined approach

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Boost by External Beam Radiotherapy

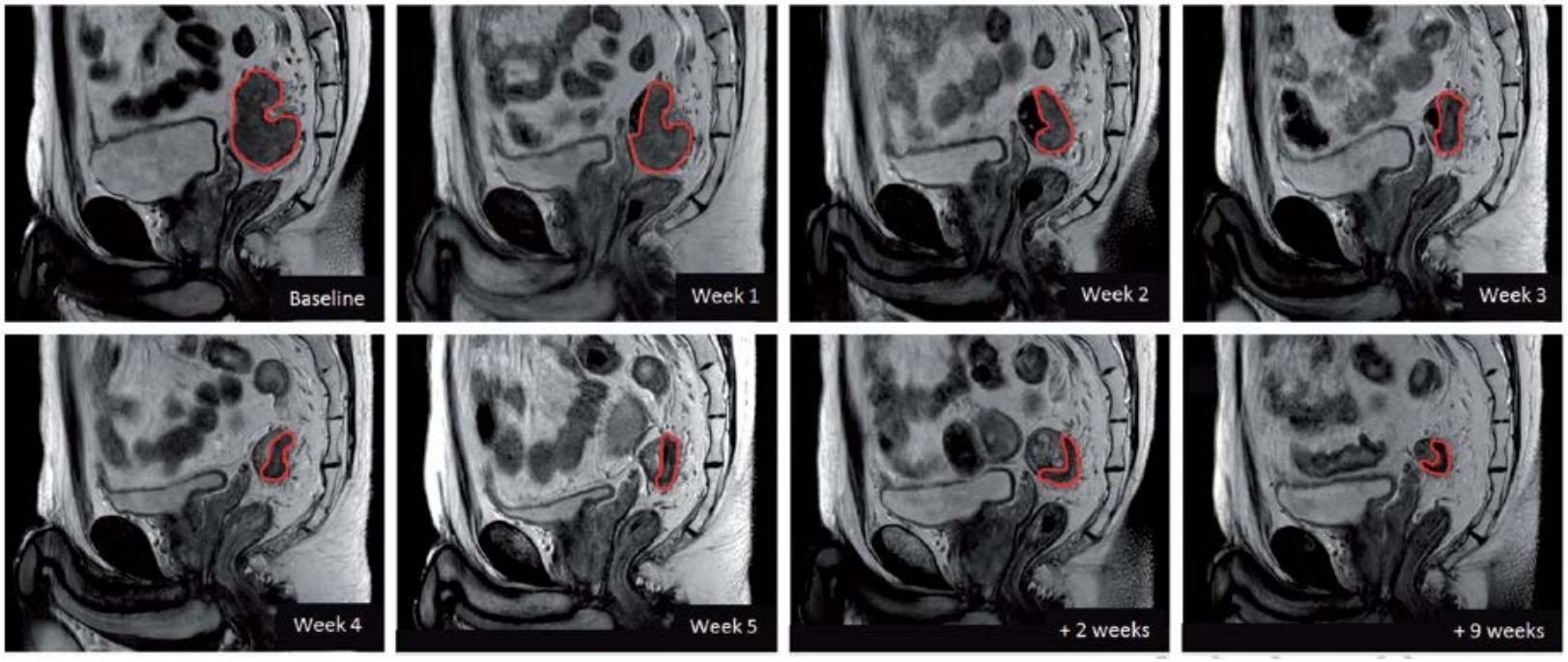
EBRT boost strategies:

ORIGINAL ARTICLE

Tumor volume regression during preoperative chemoradiotherapy for rectal cancer: a prospective observational study with weekly MRI

Robbe Van den Begin[a], Jean-Paul Kleijnen[b], Benedikt Engels[a], Marielle Philippens[b], Bram van Asselen[b], Bas Raaymakers[b], Onne Reerink[c], Mark De Ridder[a] and Martijn Intven[b]

[a]Department of Radiotherapy, UZ Brussel, Vrije Universiteit Brussel, Belgium; [b]Department of Radiotherapy, University Medical Center Utrecht, Utrecht, The Netherlands; [c]Department of Radiotherapy, Isala Clinics, Zwolle, The Netherlands



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Van den Begin et al, *Acta Oncologica 2017; in press*

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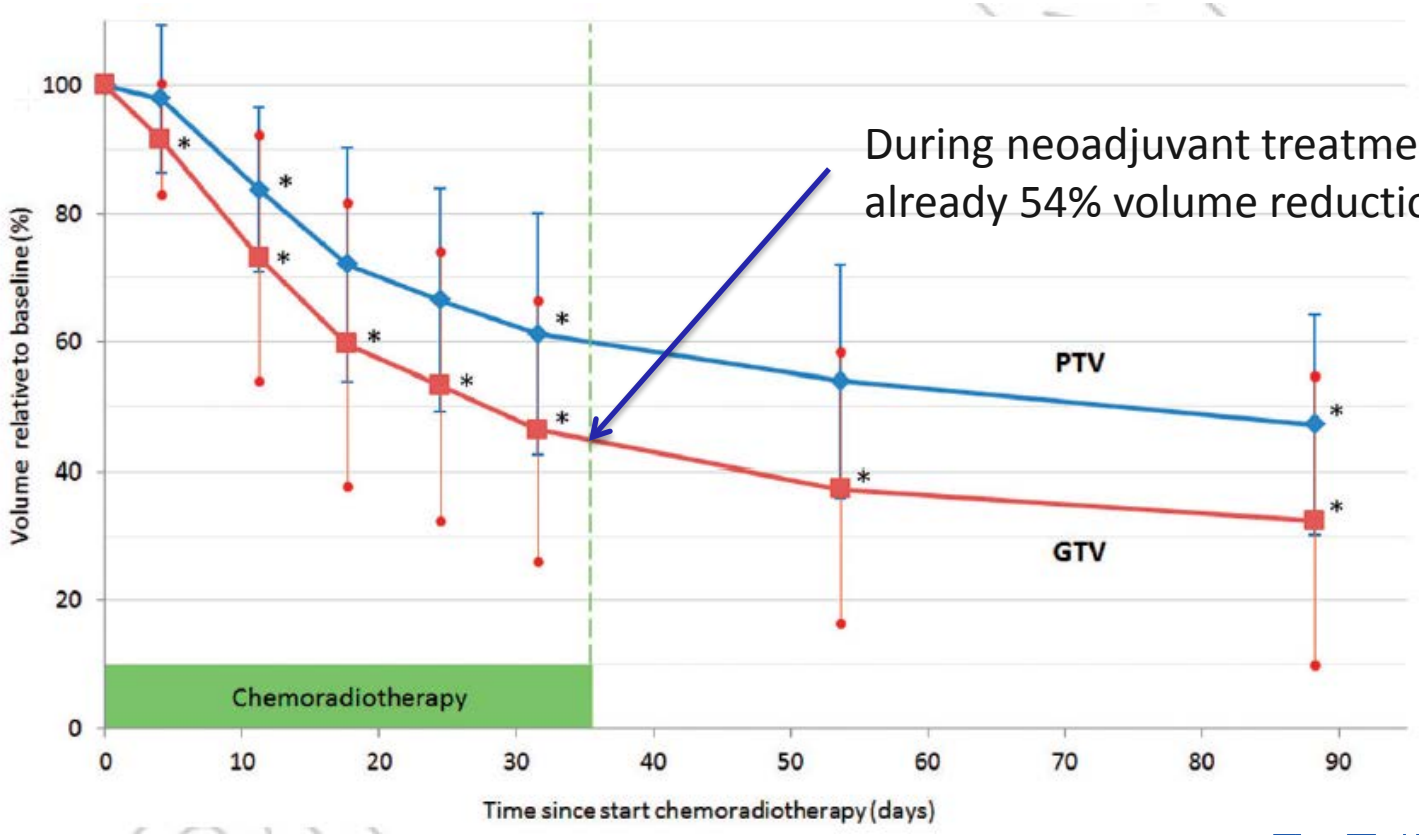

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Van den Begin et al, *Acta Oncologica 2017; in press*

Boost by External Beam Radiotherapy

EBRT boost strategies:

- Integrated (SIB = simultaneous integrated boost)
  - Pro:
    - No increase in total treatment time
    - Radiosensitizing effect of concurrent chemotherapy
  - Contra:
    - Probably some limitations in total boost fraction dose due to the concurrent chemotherapy
  - Prerequisite
    - Adaptive radiotherapy techniques
      - » MR guided radiotherapy

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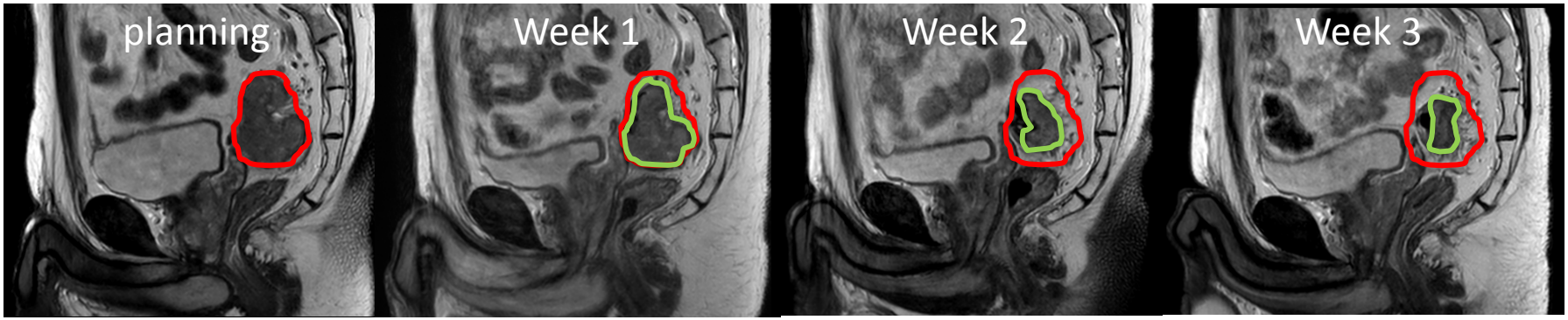
Boost by External Beam Radiotherapy

EBRT boost strategies:

- Integrated (SIB = simultaneous integrated boost)
  - Prerequisite
    - Adaptive radiotherapy techniques
      - » MR guided radiotherapy



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EBRT boost strategies:

- Sequential
  - Pro:
    - Technically less challenging
    - No limitation in fraction dose due to concurrent chemotherapy
  - Contra:
    - Increase of total treatment time

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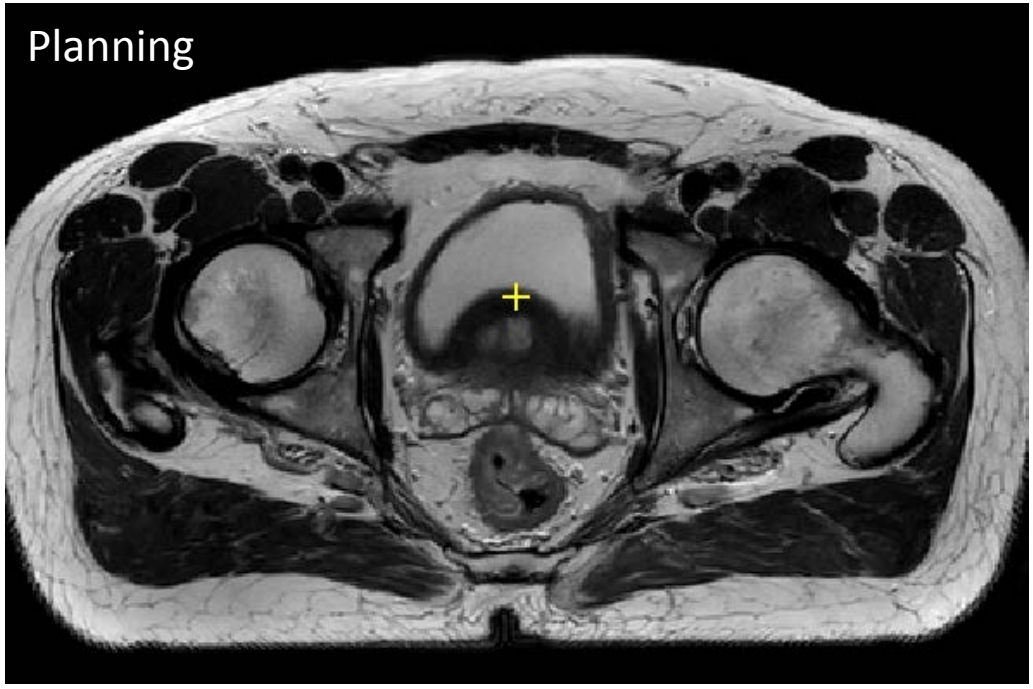
EBRT boost strategies:

- Sequential

	Volume	Target Definition
Pre	Larger	Easier
Post	Smaller	Harder



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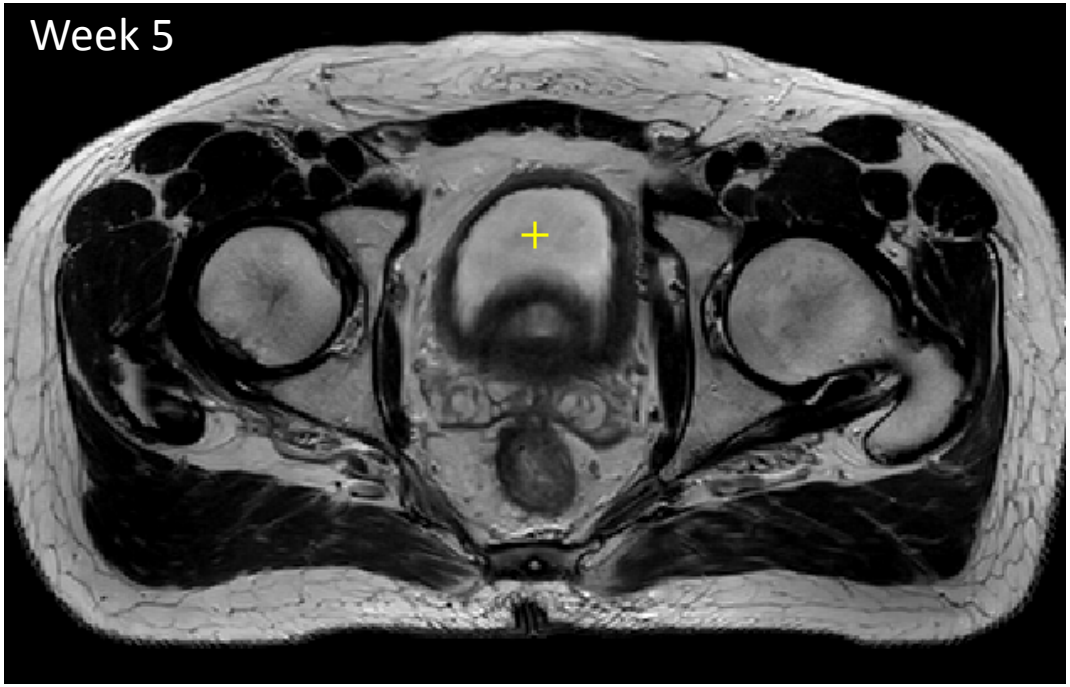

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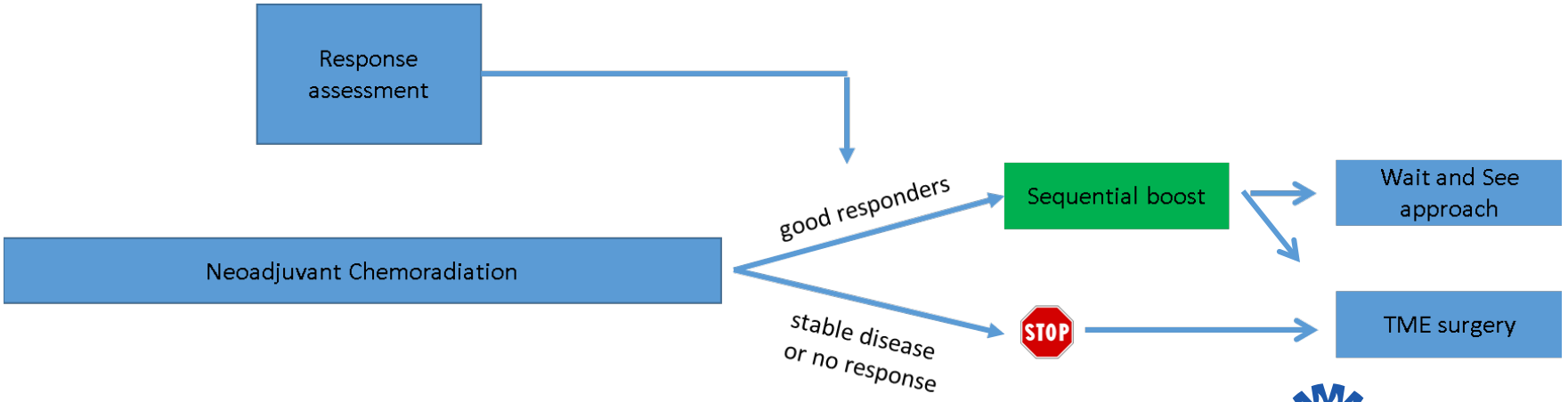
EBRT boost strategies:

- Sequential
  - Pre vs. post CRT boost
    - Post-CRT boost gives opportunity to deliver the boost only to a selected group of patients
      - » Poor responders during CRT?
      - » Already good responders with potential for organ sparing treatment?



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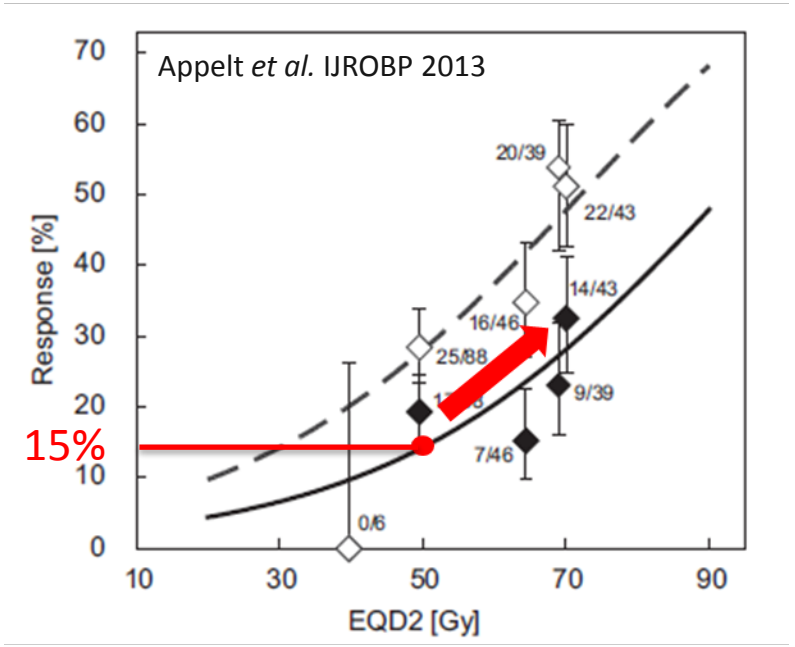
RandomizEd Controlled Trial for pre-operAtive dose-escaLation BOOST in locally advanced rectal cancer

the RECTAL BOOST trial



- Locally Advanced Rectal Cancer
- Neoadjuvant Chemoradiation
  - 50 Gy vs. 65 Gy
  - 60 patients per arm
  - Powered on pCR difference
    15 % vs. 28 %

- TME surgery 12 weeks after neoadjuvant treatment

Burbach et al, *Trials 2015* 22;16:58

Boost by External Beam Radiotherapy

Rectal BOOST Trial

- Primary Endpoint:
  - pCR
  - 2-years local recurrence-free survival after chemoradiation in patients who opted for a wait and see approach

- Secondary Endpoints:
  - Toxicity
  - Surgical Complications
  - Quality of Life
  - Disease Free Survival
  - Overall Survival

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Burbach et al, *Trials 2015* 22;16:58

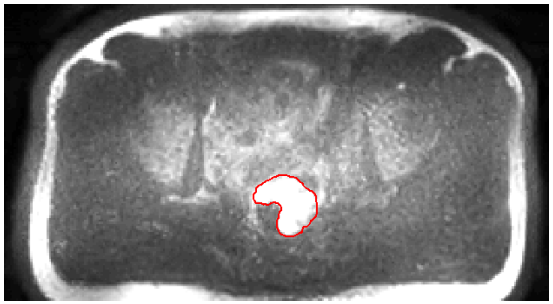
Boost by External Beam Radiotherapy

Rectal BOOST Trial

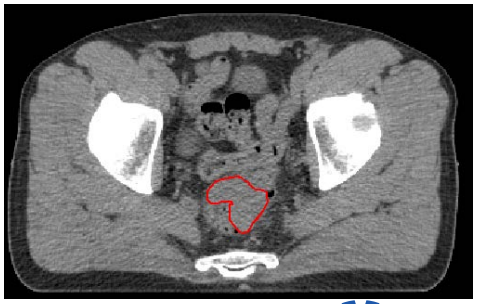
- Intervention:
  - Sequential boost prior to neoadjuvant chemoradiation
    - 5 times 3 Gy, without chemotherapy

  - Target definition based on planning MRI
    - T2w and DWI sequences

T2w image



High b-value image DWI Splice



CT

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Burbach et al, *Trials 2015* 22;16:58

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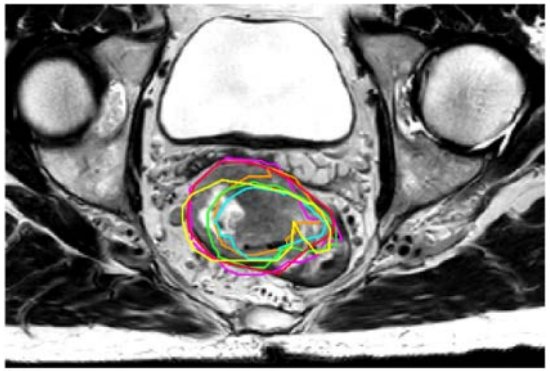
Rectal BOOST Trial

- PTV margins for boost
  - Anisotropic margins based on serial MRI scans patients with rectal cancer
    - Left-right 6 mm
    - Anterior-posterior 10 mm
    - Cranio-caudal 12 mm
  - Largest uncertainty / movement in cranio-caudal direction
    - related to rectal filling differences



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Kleijnen *et al., ESTRO 2014*

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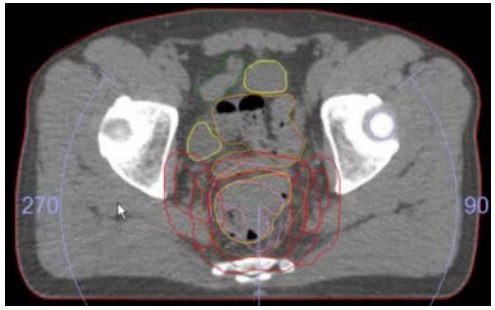
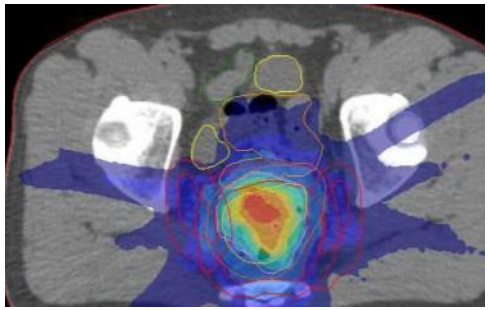
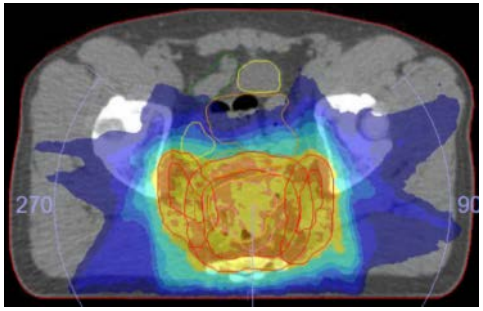
Rectal BOOST Trial

- Treatment planning

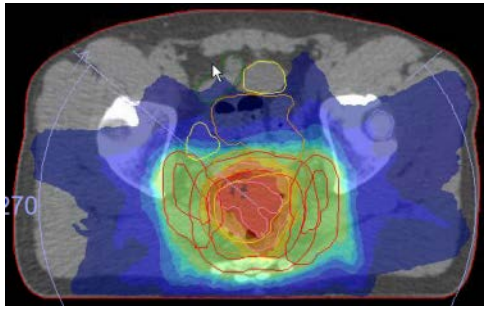


VMAT
boost
5x3 Gy
Using CRT 50 Gy plan
as bias dose





VMAT
chemoradiation
50 Gy



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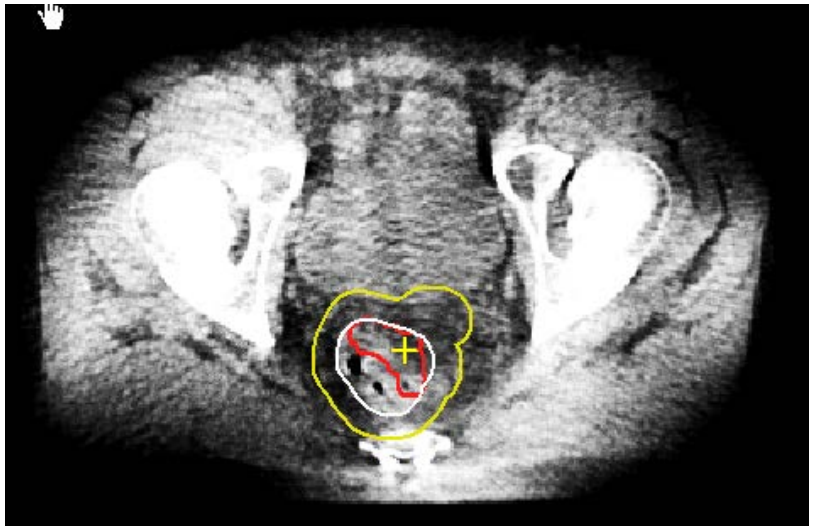
Rectal BOOST Trial

- Boost delivery
  - Position verification based on rectal wall visibility on CBCT



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Boost by External Beam Radiotherapy

Rectal BOOST Trial

- Current status:
  - Multicenter
    - UMC Utrecht
    - MAASTRO Maastricht
  - Finalizing inclusion, currently >100 /120 patients included

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MAASTRO

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Thank you for your attention!

Thanks!

- Patients
- Surgeons, oncologists, gastroenterologists, specialized nurses… from the UMCU and the referring centers

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