



Centrale Bestralingsafdeling



IMRT, what have we learned?

A systematic review in prostate cancer

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3D-CRT vs Conventional RT

“Evidence-based review of 3D-CRT
for prostate cancer: an ASTRO initiative”
(IJROBP, 2005)

3D-CRT vs Conventional RT

1. Reduce acute toxicity?
 - **Yes, reduction of acute GU/GI toxicity was suggested.**
2. Reduce late toxicity?
 - **Yes, reduction of late GI toxicity was suggested.**
3. Improve LC, DFS, OS (or subsets)?
 - **No, not found**

Aims of IMRT

1. Better target coverage / dose homogeneity
2. Better sparing of Organs At Risk
3. Increase of treatment efficacy / decrease of toxicity

Methods & Materials

- Literature search: Embase and Medline
 - 1997 – 2005
 - 531 articles (41 relevant)
 - IMRT vs. 3D-CRT
 - Outcome (treatment efficacy and toxicity)

Levels of Evidence

Level	Description
A1	Systematic reviews of phase III trials
A2	Phase III trials of high quality
B	Phase III trials of moderate quality or non-randomized comparative studies
C	Phase II trials
D	Experts opinion

Results

Level	Description
A1	Systematic reviews of phase III trials
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D	Experts opinion

Results

One level C study: Outcome (treatment efficacy)

Zelevsky

- N=772; median FU 24 months;
- Total dose 81 Gy (90%); 86.4 Gy (10%);
- Fraction dose 1.8 Gy;
- CTV: Prostate + seminal vesicles;
- Hormonal therapy (55%; 3 months)

Zelevsky

Results

3-yrs, PSA relapse-free survival**

- Favorable 92% *
- Intermediate 86% *
- Unfavorable 81% *

* No change compared with historical control

** Kupelian 2002, Pollack 2002, Nilsson 2004

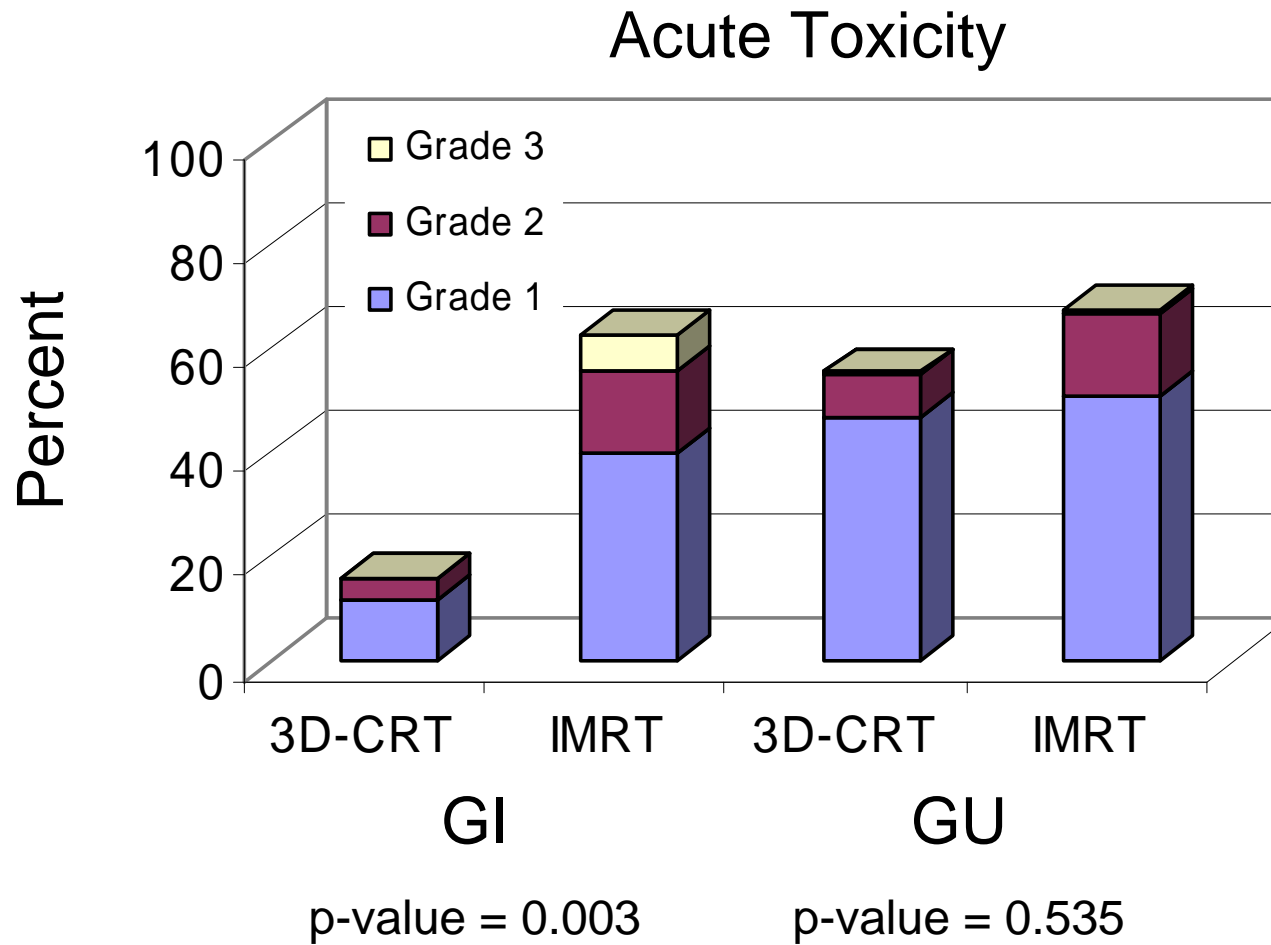
Results

Two level B studies: Toxicity

Shu

N=44;
Median FU: 23 months;
CTV: Prostate (14 x regional lymph nodes);
CTV-PTV ?? cm; TD 85 Gy;
IMRT & 3D-CRT

Results	Acute toxicity
• GI (gr 1+2 RTOG)	34%
• GU (gr 1+2 RTOG)	59%



Shu et al., Urology, 57, 102-107, 2001

Ashman

N=27;

Median FU: 30 months;

CTV: Prostate + seminal vesicles + regional lymph nodes;

CTV-PTV 1 cm (0.6 cm); TD 81 Gy; FD 1.8 Gy;

IMRT & 3D-CRT

1996 – 1999; N=14, 3D-CRT identified retrospectively

2000 – 2004; N=13, IMRT

Ashman

N=27;

Median FU: 30 months;

CTV: Prostate + seminal vesicles + regional lymph nodes;

CTV-PTV 1 cm (0.6 cm); TD 81 Gy; FD 1.8 Gy;

IMRT & 3D-CRT

Results

- GI (gr 2 RTOG)
- GU (gr 2 RTOG)

Acute toxicity

33%
40%

Results

Four level C studies: Toxicity

Zelevsky

N=772;

Median FU: 24 months;

CTV: Prostate + seminal vesicles;

CTV-PTV 1 cm (0.6 cm); Rectal wall 40%; Bladder wall 58%;

IMRT only

Results

Acute toxicity

- | | |
|------------------|-----|
| • GI (gr 2 RTOG) | 4% |
| • GU (gr 2 RTOG) | 28% |

Teh

N=77;

Median FU: 12.5 months;

CTV: Prostate;

CTV-PTV 0.5 cm; TD 76 Gy;

IMRT compared with data from Pollack 2002 (70 vs 78 Gy 3D-CRT)

Results

- GI (gr 2 RTOG)
- GU (gr 2 RTOG)

Acute toxicity

5% (60% – 66.7%)
35% (43% - 30%)

De Meerleer

N=114;

CTV: Prostate + seminal vesicles (81%);

CTV-PTV 1 cm CC; 0.7 cm; TD 72 - 78 Gy;

IMRT only

Results

- GI (gr 2 RTOG)
- GU (gr 2 RTOG)

Acute toxicity

27%

36%

Ailleres

N=16;

CTV: Prostate + seminal vesicles;

CTV-PTV 1 cm (0.5 cm); TD 78 Gy; FD 1.5 - 2.0 Gy;

IMRT only

Results

- GI (gr 2 RTOG)
- GU (gr 2 RTOG)

Acute toxicity

25%

31%

General remarks

- Little or no comparison of 3D-CRT and IMRT
- Smaller CTV-PTV margin towards the rectum
- Variety toxicity score (RTOG)

Conclusions *outcome*

- Little or no evidence found for increased treatment efficacy with IMRT
- One level C study
 - Short FU (median 24 months)
 - Use of hormonal therapy
 - Clinical value of PSA RFS questionable

Conclusions *decreased toxicity*

- Little or no evidence found for decreased toxicity with IMRT
- Two level B studies
 - Bias in patient selection
- Four level C studies
 - No comparison with 3D-CRT

What do we need for optimal treatment?

- Optimal CTV delineation:
 - using MRI */ PET-CT
- Optimal OAR delineation (rectum, anal region)
- Optimal CTV-PTV margins
 - Off-line / On-line position verification
 - Gold markers
 - Rotation of the prostate**

* Wachter et al., Strahlenther.Onkol., 178, 263-268, 2002

** Egmond et al., poster no. 1105

- Prospective registration of outcome (phase II studies)
 - Uniform toxicity score (pretreatment situation)
 - Disease free survival
 - Quality of Life (baseline score)

Take home message



IMRT should not be a ‘me too’ product

Optimize the quality of our treatment

Toxicity score

MRI

Rotations

Optimize the quality of our treatment

On-line

QOL

DFS

Off-line

Goldmarkers

CTV-PTV

Table 7. RTOG acute radiation gastrointestinal morbidity scoring criteria with the adaptations made by different authors

Author	Acute gastrointestinal toxicity			
	Grade 0	Grade 1	Grade 2	Grade 3
Cox 1995	No change	Increased frequency not requiring medication Change in quality of bowel habits not requiring medication Rectal discomfort not requiring analgesics	Diarrhea requiring parasympatholytic drugs Mucous discharge not necessitating sanitary pads Rectal or abdominal pain requiring analgesics	Diarrhea requiring parenteral support Severe mucous or blood discharge necessitating sanitary pads Abdominal distention (flat plate radiograph demonstrates distended bowel loops)
Storey 2000			Mucous discharge infrequently requiring sanitary pads Rectal pain requiring analgesics or occasional narcotics Mild rectal bleeding	Severe mucous discharge requiring extended use of sanitary pads Rectal or abdominal pain requiring frequent narcotics Gastrointestinal bleeding requiring one transfusion
Yeoh 2001	No change	Flatus with soiling without the need for a hygienic pad AND Incontinence not influencing daily activity AND Incontinence with less than 3 episodes a week	Incontinence necessitating a hygienic pad OR Incontinence impairing daily activity OR Incontinence with 3 or more episodes a week	
Nuyttens 2002	No change	Incidental bleeding not requiring admission to the hospital	Intermittent bleeding not requiring blood transfusion	Bleeding requiring hospital admission or blood transfusion
De Meerleer 2003	No change	Rectal blood loss not requiring medication AND Rectal blood loss not influencing daily activities AND Rectal blood loss with less than 3 episodes a week	Rectal blood loss requiring local medication OR Rectal blood loss impairing daily activity OR Rectal blood loss with 3 or more episodes a week	Rectal blood loss requiring transfusion or coagulation
Author	Acute gastrointestinal toxicity			
Grade 0	Grade 1	Grade 2	Grade 3	
Cox 1995	No change	Frequency of urination twice pretreatment habit Nocturia twice pretreatment habit Urgency not requiring medication	Frequency of urination less frequent than every hour Nocturia less frequent than every hour Dysuria, urgency, bladder spasm requiring local anesthetic	Frequency with urgency hourly or more frequently Nocturia hourly or more frequently Dysuria, pelvis pain or bladder spasm requiring regular, frequent narcotic Gross hematuria with/without clot passage
Nuyttens 2002		Nocturia was not scored	Nocturia was not scored	Nocturia was not scored
De Meerleer 2003			Macroscopic, but accidental hematuria	

Table 2a. RTOG acute radiation morbidity scoring criteria

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Lower GI, including pelvis	Increased frequency or change in quality of bowel habits not requiring medication/rectal discomfort not requiring analgesics	Diarrhea requiring parasympatholytic drugs (e.g., Lomotil)/ mucous discharge not necessitating sanitary pads/rectal or abdominal pain requiring analgesics	Diarrhea requiring parenteral support/ severe mucous or blood discharge necessitating sanitary pads/abdominal distention (flat plate radiograph demonstrates distended bowel loops)		Death directly related to radiation effects
Genitourinary	Frequency of urination or nocturia twice pretreatment habit/dysuria, urgency not requiring medication	Frequency of urination or nocturia that is less frequent than every hour; dysuria, urgency, bladder spasm requiring local anesthetic (e.g., Pyridium)	Frequency with urgency and nocturia hourly or more frequently/ dysuria, pelvic pain, or bladder spasm requiring regular, frequent narcotic/ gross hematuria with/ without clot passage	Hematuria requiring transfusion/acute bladder obstruction not secondary to clot passage, ulceration, or necrosis	Death directly related to radiation effects

Table 2b. RTOG late radiation morbidity scoring criteria

Organ tissue	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Small/large Intestine	Mild diarrhea; mild cramping; bowel movement 5 times daily; slight rectal discharge or bleeding	Moderate diarrhea and colic; bowel movement >5 times daily; excessive rectal mucus or intermittent bleeding	Obstruction or bleeding, requiring surgery	Necrosis/perforation fistula	Death directly related to radiation effects
Bladder	Slight epithelial atrophy; minor telangiectasia (microscopic hematuria)	Moderate frequency; generalized telangiectasia; intermittent macroscopic hematuria	Severe frequency and dysuria; severe generalized telangiectasia (often with petechiae); frequent hematuria; reduction in bladder capacity (<150 cc)	Necrosis/contracted bladder (capacity <100 cc); severe hemorrhagic cystitis	Death directly related to radiation effects

- Meerleer tox Zel.
 - GI 21%
 - GU 22%

A.

Acute Toxicity

