Practical implementation of MR-guided RT: pancreatic SBRT as an example site

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~3.500 new patients / year
MR-guided RT using the MRIdian

MR-guided radiotherapy system (ViewRay, USA)
- Split core MRI 0.35 Tesla
- Radiation delivery system
  - three cobalt sources
  - capable of IMRT delivery

Pelvic lymph node 5 x 7 Gy

1st clinical treatment May 4th 2016
SMART @VUmc

**SMART**

*Stereotactic*  
*MR-guided*  
*Adaptive*  
*Radiation Therapy*

- Make **full use** of MRIdian capabilities
- Hypofractionation: SBRT/SABR
- Clinical potential benefits:
  - Increase biological dose
  - Minimise toxicity, preserve QoL
  - Organ-sparing SBRT (rectum, kidney)
  - Complex SBRT indications (pancreas)
SMART @VUmc

**SMART**

Stereotactic

MR-guided

Adaptive

Radiation Therapy

High dose/fraction (high biological dose)

Precise setup and guidance (3 mm margin)

“Plan of the day” based on current anatomy
SMART for pancreatic cancer

N=786 (APR 2017)

- Prostate: 32%
- Pancreas: 16%
- Lung: 13%
- Liver: 11%
- Lymphoma: 2%
- Pelvic LN: 3%
- Abdomen: 3%
- Breast: 1%
- Kidney: 6%
- Adrenal: 8%
Current “standard” for LAPC

LAPC: Poor prognosis group, without international gold standard trt

Conventional EBRT
28 x 1.8 Gy + gemcitabine
Large mobility margins needed
OAR tolerance dictates fractionation
Conventional CT-RT for LAPC

@VUmc, we rarely used radiation for LAPC
Hypofractionation ?
Ample (non-randomised) literature on SBRT for PC:

• Efficacy higher with biological doses above 70 Gy (control, survival)\(^1\)

• Duodenal toxicity (bleeding, strictures, perforation) remains problem

• Reported rates of acute and late grade ≥3 GI toxicity up to 12.5% and 22.3%, resp. \(^2\)

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\(^1\) Krishnan S, et al, IJROBP, 2016

\(^2\) De Bari Berardino, et al; Crit Reviews in Oncol and Hematol, 2016
End 2015: discussion on trial with SBRT for LAPC

AND

Simultaneous discussion on purchasing MRIdian
Cross-atlantic randomized controlled trial comparing outcome in survival after systemic plus focal therapy for inoperable pancreatic cancer: radiotherapy versus irreversible electroporation.
Study population:

- Patients with histologically proven adenocarcinoma (AJCC stage III)
- No contra-indications for MRI
- No nodal disease
- No local ingrowth in surrounding organs

SBRT fractionation schedule:

5x8 Gy@ 100% on non-consecutive days (BED ~72 Gy$_{10}$)
MR-guided SBRT... a big step

- If we used SBRT for LAPC, the fractionation had been 3 x 8 Gy
- Target definition was always difficult, even when using 4DCT scans
- Maybe because of these margins, 3 x 8 Gy was not without toxicity....
- So, the step towards 5 x 8 Gy was somewhat progressive for us
And... as always, to make things more stressfull, the first patient referred to us for MR-guided SBRT had a large LAPC with local ingrowth in stomach and duodenum (therefore outside the Crossfire trial)
72 year old patient

11-'15: loss of appetite, weight loss, fatigue, abdominal pain

**Analysis**: adenoca in the head/corpus of the pancreas, Ø 5 cm, N0, invasion in duodenum and stomach, extended vasculair involvement.

**Palliative CT**: after 4 cycles FFNX regression of pain, but PD on CT scan

Discussed for the CROSSFIRE study, but not suitable due to the tumor size and invasion

*So, referred for (palliative) SMART*
How to perform MR-guided SBRT or SMART?

- **Basic principle:** prolonged palliation....
- Do not want to harm patients, in particular as SBRT is no standard treatment

**Use all available options of the MRIdian:**

- Advanced set-up using HR MRI scans
- Fractionate appropriately; *in this case 5 x 7 Gy*
- Avoid high doses in surrounding OAR in baseline plan
- Use daily adaptation to make sure that this happens for each fraction
- Find a system for gated delivery (markerless)
Advanced set-up using HR MRI scans

Routine CT without iv. contrast (image quality of CBCT worse):

Need for setup with markers!

Image on MRIdian (0.35 Tesla):

Soft tissue setup based on tumor possible.
GTV:

- Gross tumor volume is contoured on the planning MRI
- Elective lymph nodes regions are not part of the target volume

Planning target volume (PTV) = GTV + 3 mm

A \( PTV_{opt} \) is created = PTV minus the organs at risk

\( PTV_{opt} \) will receive 40 Gy/5 fractions @ 100%

Case-specific: dose was restricted because of gastric and duodenal invasion
Advanced set-up using HR MRI scans
Advanced set-up using HR MRI scans

- Target and OAR contouring on a planning MR-scan
- 17 sec MR-scan in shallow inspiration BH
- Repeat MR-scan and set-up performed by GTV alignment
Adaptive process feasible and fast

- For SBRT, the high dose region around the PTV is important for toxicity
- A planning procedure was developed using rings up to 3 cm around the PTV
- Only parts of organs within these rings need to be adjusted to the anatomy
Optimal normal organ sparing prevails (driving force for planning)
Daily adaptation
Re-optimizing the original plan and creating a plan of the day
Effect of re-optimization in PC
Effect of re-optimization in PC
Blue dots: Indicate plans fulfilling the institutional constraints

**Vertical axis:** PTV coverage

**Horizontal axis:** High dose volume to the OAR
Red dots:
Indicate non-adapted plans with insufficient PTV coverage and/or exceeding OAR constraints

The original plan projected on the current anatomy
Almost all plans comply with high-dose volume constraints, while even improving target coverage.
Patient-controlled breath-hold gated RT
In real-time the projected GTV within the PTV on a sagittal tracking image derived from the MRIdian console.
Confronting seeing their own tumor?

- Was it difficult to control the target by holding your breath?
- Was it confronting to see your tumor during the treatment?
- Did you like having an active role during treatment?
MR-guided tumor setup

Adaptive planning

Online guidance

Gated delivery (markerless)

A single fraction of 7-8 Gy can be delivered within 20-30 min
Patient-controlled breath-hold gated RT

- Gating efficiency defined as calculated versus actual delivery time
- Mean gating efficiency 67% (range 43-79%)
- Observed learning curve for patients
SMART for pancreatic cancer

**Pre-treatment:**
- Patient positioning
- Pilot scan
- HR breath-hold scan
- Contouring (tumor/normal organs)
- Plan generation / QA

**For each fraction:**
- Patient positioning
- Pilot scan
- HR breath-hold scan
- Matching with baseline MR (on tumor)
- QA
- Positioning verification
- Re-optimisation of the plan
- Plan prediction
- Deformation and adaptation of normal organs
- Treatment delivery in breath-hold periods
The mean duration of SMART delivery was 61 min (125 fx) including all SMART steps from patients entering and leaving the treatment room.
Acceptable for the patients?

Treatment duration tolerable?

- Yes
- A bit
- Moderate
- Unacceptable
Coming back to our first patient:

As early toxicity: mainly fatigue and after the first fraction an increase in pain, responding well on dexamethasone and antiemetics

> always pre-treatment with dexa and antiemetics
> from three times a week to twice a week
> patients in pain @consultation; increasing painkillers

All his complaints subsided two weeks after completion of treatment
What is the impact of this treatment?

After this initial experience, I felt some uncertainty about what to expect with this treatment schedule.

In order to understand the impact of SMART on my patients, I ensured a careful follow-up, “meaning that I spent as much time on the MRIdian as on the phone with the patients afterwards.”

Why?

Primary goal of SMART was to not cause excessive toxicity (and try to improve local control).
Preliminary clinical experience

• SMART was delivered in **25 pts** (May 2016-March 2017)
• 12 female; 13 male
• Mean 66 years; (range 36-87)
• 23 pts with **LAPC**, 2 pts with **local recurrence**
• All patients treated with upfront chemotherapy (usually FOLFIRINOX)
• All treated with **5 x 8 Gy/2 weeks**
• Two pts with local ingrowth (stomach) treated with 5 x 7 Gy/2 weeks
Acute toxicity

Grade 2
Pain: Grade 2 (N=1); Grade 3 (N=1)
Fatigue: Grade 2 (N=9); Grade 3 (N=1)

Grade 3

Grade 4

Grade 5
During follow-up:

- Repeat CT scan@9 months of FU after SMART showed stable disease, he was without complaints and was working

- However, 12 months after SMART, which is in line with LAPC, the disease is not stable with an increasing marker; start FFNX
Curb your enthusiasm

- Started relatively blank; not much experience with SBRT for LAPC
- Strong confidence in limited side effects with SMART
- No local recurrence yet
- Much enthusiasm about SMART itself
- But....it remains a dismal disease and we have to cope with patients showing PD elsewhere
Thank you for your time!

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