Changing Paradigms in Radiotherapy

Marco van Vulpen, MD, PhD

Towards the elimination of invasion

Two Hundred Years of Surgery

Atul Gawande, M.D., M.P.H.

Meanwhile, the practice of surgery itself will continue to change. Prognostication is a hazardous enterprise. But if the past quarter century has brought minimally invasive procedures, the next may bring the elimination of invasion. One feels foolish using terms like nanotechnology — I haven’t the slightest idea what it really means or can do — but scientists are already experimenting with techniques for combining noninvasive ways of seeing into the body through the manipulation of small-scale devices that can be injected or swallowed. Surgical work will probably even become fully automated.
NIH opinion on the future of oncology

Twenty-five years from now, I hope that we won’t perform any more open surgery. There would be no need to essentially take the risk of full exposure of the human body to go to a targeted region that needs to be affected.

Elias Zerhouni, former director NIH

Example: breast cancer

Examples

• Established example: larynx cancer
  – By chemoradiation preservation larynx:
    • Speach
    • Swallow
    • Infections
    • etc

• Example current development: rectal cancer
  – By chemoradiation preservation rectum:
    • Control of defecation
Mission statement:
Providing minimal invasive MRI guided cancer therapy

Collaboration:
• Radiotherapy, Radiology, Nuclear Medicine
• Image Science Institute (IMAGO)
• Within UMC Utrecht Cancer Centre

(Radio-)therapy (UMC Utrecht) goes MRI

• Tumour quantification and characterization
• MRI simulation: delineation / “CT” output for planning
• MRI guidance
  – MRI-guidance external beam
  – MRI-guided brachytherapy
  – MRI-guided HIFU
  – MRI-guided protons
  – MRI-guided radio-embolization
• MRI treatment response assessment
4D MRI + optical flow tracking

13 min to obtain dataset

ESTRO 2015 Stemkens et al

CO_RASOR: CT-like MRI

Courtesy P. Seevinck
MRI and linear accelerator

Artist impression

Prototype MRI accelerator

1.5 T diagnostic MRI quality

No impact of beam on MRI

Successful test clinical MRL system

Clinical MRI linac system:
10-10-2014 test
Simultaneously deliver Radiation and make MRI
MRI-guided brachytherapy

- A shielded treatment room with:
  - 1.5 Tesla MR scanner
  - MR compatible HDR afterloader
  - MR compatible applicators, needles, tubes
  - MR compatible instruments/robotics

MRI robotic implant system

- Needle
- Needle
- Markers
Changing Concepts in Radiotherapy

Radiotherapy is changing essentially

From X-ray-based planning to MRI-based planning

From no movement correction to adaptation

Concluding: Current Radiotherapy is of high precision / high quality
Techniques versus approach

Technical radiation delivery techniques:
- Conventional / Conformal radiotherapy / …
- IMRT / VMAT / Tomotherapy / …
- Cyberknife / Radiosurgery / …
- Protons / Carbon-Ions /
- Brachytherapy / …
- etc …

What do we want:
100% cure, 0% toxicity, 100% Quality of Life

Treatment approach: Image Guided RadioTherapy (IGRT)
- spatial control of the dose distribution
- Inhomogeneous dose distribution
- based on the 3D tumor-characteristics
- Individualized treatment

Breakthrough: CT-linac

Changing concepts:

<table>
<thead>
<tr>
<th>History</th>
<th>Tendency</th>
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</thead>
<tbody>
<tr>
<td>Fractionated</td>
<td>Hypofractionated</td>
</tr>
<tr>
<td>Homogeneous dose</td>
<td>Inhomogeneous dose / stereotaxy</td>
</tr>
<tr>
<td>Dose prescription ICRU</td>
<td>Maximum dose less important, if safe</td>
</tr>
<tr>
<td>Radioresistant tumors</td>
<td>Probably do not exist (e.g. kidney)</td>
</tr>
<tr>
<td>Etc</td>
<td></td>
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This makes Image Guided Radiotherapy a real alternative for surgery
Motion incorporated plan optimization

Future plans: Prospective motion incorporated IMRT optimization
MRI-linac possibilities for current clinical practice?

**Theoretical gain?**

- **General:** Decrease morbidity
  
  **Reason:** Intra-fraction control
  
  Movement of tumor and normal tissue, deformation, shrinkage

But, technical challenging / complex developments,

- RF coils, 2D or 3D tracking, table steering, intrafraction automated contouring, intrafraction planning or maybe a library of plans, questions on who will decide when it is safe to irradiate, on a dose range to achieve or maybe on a maximum or minimum dose to achieve, fractionation, etc.

- Safely deliver a higher dose to GTV, if required
- Current fractionation may be reduced for some sites.
- Biology may become visible.
- New treatment sites might become available.

**Thought experiment: MRI-linac for renal cancers**

- **Current standard of care:** Nefrectomy if tumor > app. 3cm
- Renal cancers (2% of cancers) were considered radio-resistant:
  - Normal kidney tissue is very sensitive for radiation damage
  - Kidney large movements
  - Other normal tissue is in close proximity (bowel, liver)

It might be valuable to re-examine radiotherapy as a possible treatment for other indications too.
Changing concepts?

- Fractionation rules
- Why homogeneous dose
- Why set minimum or maximum dose
- ICRU 50/62/83
- Radioreistance
- Alpha/Beta
- Retreatment rules (BED)
- Profession as radiation oncologist?
- Contouring by radiation oncologists?
- GTV / (CTV?) / normal tissue
- Etc...

A future treatment may look like….

- Pre-treatment
  - Optimal information on anatomy, biology, movement
  - Planning which deals with patient specific uncertainties
- Treatment
  - 45 minutes of treatment time
  - Look with optimal soft-tissue contrast
  - Adapt for movement of tumour
  - Dose accumulation / Anatomy of the day important:
    - If normal tissue is too close: stop treatment at safe level (e.g. 10Gy) and come back another day
    - If not, treat until maximum time has elapsed. Maximum dose less important if safe (e.g. 40Gy)
- Post-treatment
  - Optimal information on biology to check response
  - Re-treatment if required, same rules as above
How about the Mouldroom?

Discussion: Vote please
1. With optimal treatment guidance no additional fixation required
2. Extreme hypofractionation requires additional stability measures

Shift towards treatment in MRI: additional requirements?
   MRI compatible, small bore, etc

Changes in patient logistics: where to place the mouldroom?
   Location, on spot?, keep fixation on all imaging, store blue bag for everyone?, etc

More extreme moulding: like tongue? Due to limited fractions and high GTV doses?

Paradigm shift / disruptive technology

• From "elective" to "ablative"
• MRI-based adaptive hypofractionated radiotherapy
• Towards organ sparing approaches, eliminate invasion

• Redefine radiotherapy?: discuss margin and CTV-PTV concepts, fractionation rules, dose homogeneity, α/β assumptions, radio-resistance, re-evaluation of indications, re-treatment, set a dose, etc.