Clinical case: Head and Neck

Course on Advanced Radiotherapy Techniques

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Clinical questions:
- prevent complications
- improve TCP

Delineation of target volumes: What is the optimal imaging technique? Validation of imaging essential

Advanced radiation techniques for Head & Neck cancer: rationale

Criteria (Potters)
- irregular shaped target volume (oro-nasoph, sinonasal cavity)
- narrow margin of volume of interest to critical structures (elective node area - parotid glands, submandibular glands; tumor - spinal cord, optic pathway, cochlea, swallowing structures)
- (partially) previous irradiation (second tumors)
- other techniques are insufficient
- dose escalation (primary radiotherapy - organ preservation)

Advanced techniques for H&N: prerequisites

- Image guided RT: determine GTV by CT/ MRI/ PET
- Delineate normal structures
- Margins between GTV – CTV – PTV, “organ” movement
- Normal tissues: dose-complication curve
- IMRT: inverse – forward
  SIB: simultaneous integrated boost (SMART)
  penalty setting tumor/ normal tissues
  Rapid Arc – Vmat
- Protons / MRI accelerator

CT/MRI/PET: in same mould
accurate co-registration with planning CT using rigid mutual information
delineation: MRI:above hyoid; CT: under hyoid

xerostomia
dry mouth, burning sensation, thirst, prostheses difficulties, difficulties with eating, swallowing, speech and sleep, altered taste and eating habits, sticky saliva, impaired sensitivity to oral infections, caries

Locoregional recurrence after S+RT
UMCU: FDG-PET Image analysis: ’03-’10: n=329
Qualitative: visual accounting for physiological uptake

Combined CT/PET, UMCU ’03-’10
Field/ dose adjusted (n=212/ 329 analysed), Percentage

- Local Scatter
  - CT: tumor invisible
  - Neck
  - PET: no boost
  - PET+: boost
  - M/second tumour

Delineation of GTV – CTV – PTV
Most crucial!

- Hong et al heterogeneity in H&N target delineation T2N1M0 tonsilar ca
- 20 delineators, internationally

Interobserver reliability of CT GTV supraglotticby 8 experienced readers
Mukheyni et al Cancer 2005

N=20 CT scans, median volumes for each group (white bars), dashed line: range of the volumes, p=0.02
Conclusion: GTV measurements were reliable and reproducible

Same data, same selection (20 supraglottic ca), same 8 readers Cooper et al, IJRad Oncol Biol Phys 2007

Average proportion of overlap was 0.532
Conclusion: estimation of tumor shape is imprecise, even for experienced physicians, limits the use of smaller fields

Tumour delineation: The weakest link in the search for accuracy in radiotherapy
Delineations uncertainties in general larger than set-up errors
Rasch et al Radiat Oncol. 2010 Mar 15;5:21
Pathologic validation of laryngeal carcinoma

H&E - 3D - MRI
coupes specimen CT T1w gd T2w FDG-PET

Pathologic validation: laryngeal cancer
Inconsistencies in delineation

<table>
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<th>Average delineated volumes and GTV-path coverage (N=10)</th>
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<td>Pathology</td>
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<td>GTV volume (ml)</td>
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<td>GTV coverage (%)</td>
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- overestimation of the GTV
- Underdosage of GTV
- Normal tissue damage

Margins: Microscopic extension? (CTV)
Movement? (PTV)

GTV: 12 cc - CTV: 55 cc – PTV 139 cc

PTV margin: dep. mould, interfraction movement
Ls: standard mould
Rs: individual mould: margin from 5 (s) to 3 mm (i)

Larynx: margin reduction: for CTV: 1 to 0.5 cm,
movement: 1 to 0 cm, PTV: 5 to 3 mm; 69.5 Gy/ 5 weeks

- GTV
- PTV_{new}
- PTV_{old}

margin reduction – late toxicity,

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<th>NTCP Swallowing Muscle</th>
<th>NTCP Submandibular Glands</th>
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<td>Group 1</td>
<td>Group 2</td>
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Group 1: local RT only (3) (69.5 Gy – 40 fractions)
Group 2: local and elective RT level II – IV Re en Li (10) (47 Gy – 25 fractions)
Group 3: local and curative RT on nodes (6)
Black: "standard" margins; Grey: reduced margins
• Delineation normal structures
• Dose response curves

Submandibular gland delineation: MRI-sialography
Houweling et al. Radiat Oncol 2010:5:239-243

-Sagittal MR sialography images of 2 patients with the clinical CT/MRI-delineation (solid line) and the MRI-delineation (dotted line)

Delineation of swallowing structures

Cochlea: delineation

Delineation of the chiasma
IMRT penalty setting, based on NTCP-data. 400 parotids combined results UMCU/Michigan

Swallowing complaints: penalty setting

IMRT in practice

Settings used for optimization in PLATO/ITP, setting for parotid glands is varied

Forward vs. inverse treatment planning for IMRT

IMRT: UMCU oropharynx, inverse

n=10, mean dose to parotid glands

inverse: 1/ better target coverage, 2/ 3-11 Gy lower dose to parotids

Significant dose reduction parotid gland using IMRT: 44.1 - 33.7 Gy

Significant reduction in complications (flow < 25%) using IMRT:

- 6 weeks: 87% vs 55% \( p = 0.002 \)
- 6 months: 81% vs 55% \( p = 0.04 \)
- 12 months: 83% vs 41% \( p = 0.003 \)
IMRT vs. conventional

Randomized study nasopharynx: parotid flow
Conventional radiotherapy (CRT) for H&N tumors: 40% moderate or severe xerostomia after 5 yrs

Intensity-modulated radiotherapy (IMRT) reduces mean dose to parotid glands

Kam MK et al. JCO 2007

Randomized study nasopharynx: Quality of life questionnaire: gr 2-4 xerostomia
Treating physicians

Patients

Kam MK et al. JCO 2007

glandula submandibularis underestimated?

Submandibular dose response curve
UMCU: advanced IMRT
Submandibular gland sparing
On-going prospective study

Ann Arbor Michigan

Results: NTCP for submandibular gland
UMCU

Sparing contralateral submandibular gland
IMRT Oropharynx, planning study, UMCU
Houweling Rad Oncol 2008

Plan B, 2 mm

A: no sparing; B-E sparing; margin CTV-PTV 5 or 2 mm
B: PTV elect >95%, C: PTV elect >90%, D: planned dose subm gland <40 Gy
The potential benefit of swallowing sparing intensity modulated radiotherapy to reduce swallowing dysfunction: An in silico planning comparative study (n=30, bilateral RT) © van der Laan et al. Radiat Oncol 2011

• Standard IMRT plan
• Optimization based on dose to superior and middle swallowing muscles, supraglottic larynx
• Equal dose to parotids/ subm
• Swallowing muscles sparing RT: mean expected 9% less grade 2-4 RTOG score

Maximum dose for sinus ethm. Comparing conventional, 3D-CRT, IMRT

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<tr>
<th></th>
<th>conventional</th>
<th>3D-CRT</th>
<th>IMRT</th>
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<tr>
<td>Left optical nerve</td>
<td>71 Gy</td>
<td>61 Gy</td>
<td>56 Gy</td>
</tr>
<tr>
<td>chiasma</td>
<td>52 Gy</td>
<td>43 Gy</td>
<td>53 Gy</td>
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Microscopic incomplete resection of recurrent pleomorphic adenoma: PORT: 25 x 2 Gy, Cone beam, 5mm leaves

Conv. 4 (wedge) field  IMRT 5 field, 76 segments

SMART vs. sequential, T3N1 oropharynxca, ulcus 5 cm tonsil Left, til base of tongue, trigonum 20120431

Sequential: 95%: 46 Gy and 24 Gy boost
SMART 95%: 54/49 (69 Gy)

Proton therapy: superior to photontherapy in H&N ca.? Planning study in 10 patients

Proton therapy: superior to photontherapy in H&N ca.? Planning study in 10 patients

However: in literature no clinical evidence of superiority

Comparing IMRT techniques:
all: excellent quality, IMRT best sparing, V-mat fast, V-mat is most efficient. Stieler et al Rad Oncol 2011: 388-393

Advantage of adv rad techniques depend largely on the quality and the interpretation of the imaging used for delineation and guidance

CT  MRI  MRI - accelerator
**Conclusions: Adv RT techniques for H&N cancer**

- High quality images and extensive experience essential for delineation of normal structures and tumor extension
- NTCP-data essential for the penalty setting of the normal structures
- Knowledge of margins needed for CTV essential, derived from pathology studies
- With (forward) IMRT significant improvement in mean dose on parotid glands, spinal cord, cochlea ongoing studies on sparing submandibular gland and swallowing structures, ....

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**DVH for optimized dose distribution oropharynx**

Comparison between B = 0 T and B = 1.5 T


**Delineation of nerves and nodes: improved MRI techniques: MRI / PSIF or T2-FFE**

- fat, blood and muscle suppression
- 3D, all directions 0.5 mm
- T2 and diffusion weighted (no AD calculation)