Something about treatment of head and neck cancer and the need for rehabilitation

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Head and Neck Cancer

- >1,100 new cases in Denmark per year
- prevalence 14,000 patients

Etiology:
- Tobacco
- Alcohol
- Infection (EBV, HPV)
Head and Neck Cancer

- Most tumors have origin in the mucosal epithelium (squamous cell carcinoma)
- Spread to regional neck nodes, seldom as distant metastasis.
- Loco-regional treatment (with organ conservation).
- Many vulnerable critical structures and functions in the area.
Treatment of head and neck cancer is heterogeneous (and influenced by local tradition):

• Surgery alone
• Radiotherapy alone
• Pre- or postop-radiotherapy
• Surgery combined with chemotherapy
• Radiotherapy combined with chemotherapy/EFGr inhibitor
• Radiotherapy combined with hypoxic modification
• Radiotherapy with different dose/fractionation
• All thinkable combinations of the above
There is no international consensus – and there is no strong evidence to favour one strategy against another.
Radical Head & Neck Surgery

Residual tumor?
Morbidity?
Why not try with radiotherapy?
Head and Neck radiotherapy: Conservation of organs and functions - but not without side effects
DOSE

0%
20%
40%
60%
80%
100%

PROBABILITY

risk of complication
tumor control

DOSE

30 40 50 60 70 80 90

PROBABILITY

100%
80%
60%
40%
20%
0%

30 40 50 60 70 80 90
Primary RT of HN Cancer

- Reduced RT time
- Accl fx
- Hypoxic modification of RT
- Changed RT-Surg balance
- Neo-adjuvant Chemo-RT
- Sunlral RTvolume IMRT
- Basic “virtues” Waiting time etc.
- Con-committant Chemo-RT
- Biological modifiers Anti-EGFr
- Smaller RT dose Hyperfx

Better diagnosis and imaging

Dahanca 1
Dahanca 2
Dahanca 5
Dahanca 7
Dahanca 6
Dahanca 10
Dahanca 11
Dahanca 9
Dahanca 13
Dahanca 15
DAHANCA.dk
The DAHANCA strategy: progression through consecutive clinical trials

**Advantages of Hypoxic Modification**

- **DAHANCA 5 (1986-1990)**: Benefit of hypoxic modification
- **DAHANCA 2 (1979-1985)**: Loss by split-course (prolonged) treatment time

**Results**

- **Loco-regional control**
  - Standard 1977: 22%
  - Standard 2010: 41%

**Survival**

- **Disease-specific survival**
  - Standard 1977: 60%
  - Standard 2010: 62%

**Visual Elements**

- Graph showing time after treatment (months) and loco-regional control (%)
- Graph showing disease-specific survival (%) over time

**Conclusion**

Better tumor control gives more long-term survivors with risk for more (late) problems.
Acute radiation related morbidity
Acute radiation related morbidity

Severe skin reaction

It is painful, 2/3 of pts gets morphine.

Severe mucositis

Most have eating problems (weight loss)
Weight change during radical RT (>60 Gy)

n = 449

J Johansen, G Bjerg Petersen et al 2009
DAHANCA 25A

CIRRO-IP010309

Styrketræning kombineret med kosttilskud som intervention til genopbygning af muskelmasse efter strålebehandling for hoved-hals cancer
Late morbidity after head and neck irradiation

- Xerostomia
- Dysphagia
- Under- and malnutrition
- Trismus
- Dental problems, osteo-radionecrosis
- Atrophy of mucous membranes
- Pain
- Neurological problems, incl. visual, auditory, gustatory and olfactory dysfunction
- Hypothyroidism
- Disfigurement
- Laryngectomy
- Secondary cancer
Late morbidity
Prevalence of grade 2-3 (n=1420)
Observer assessed

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Short Name</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nail changes</td>
<td>Nail changes</td>
<td>Discoloration; ridging (koilonychias); pitting</td>
<td>Partial or complete loss of nail(s); pain in nailbed(s)</td>
</tr>
<tr>
<td>NAVIGATION NOTE: Petechiae is graded as Petechiae/purpura (hemorrhage/bleeding into skin or mucosa) in the HE.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>Photosensitivity</td>
<td>Painless erythema</td>
<td>Painful erythema</td>
</tr>
<tr>
<td>Pruritus/itching</td>
<td>Pruritus</td>
<td>Mild or localized</td>
<td>Intense or widespread</td>
</tr>
<tr>
<td>ALSO CONSIDER: Rash/desquamation.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash/desquamation</td>
<td>Rash</td>
<td>Macular or papular eruption or erythema without associated symptoms</td>
<td>Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering &lt;60% of body surface area (BSA)</td>
</tr>
<tr>
<td>REMARK: Rash/desquamation may be used for GVHD.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash: acne/acneiform</td>
<td>Acne</td>
<td>Intervention not indicated</td>
<td>Intervention indicated</td>
</tr>
<tr>
<td>Rash: dermatitis associated with radiation</td>
<td>Dermatitis – Select</td>
<td>Faint erythema or dry desquamation</td>
<td>Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema</td>
</tr>
<tr>
<td>Rash: erythema multiforme (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis)</td>
<td>Erythema multiforme</td>
<td>—</td>
<td>Scattered, but not generalized eruption</td>
</tr>
<tr>
<td>Rash: hand-foot skin reaction</td>
<td>Hand-foot</td>
<td>Minimal skin changes or dermatitis (e.g., erythema) without pain</td>
<td>Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function</td>
</tr>
</tbody>
</table>
Consequences of side effects

• Fatigue
• Inability to eat in a social context
• Social isolation
• Loss of income
• Sexual problems
• Depression
• Inability to communicate (speak)
• Reduced quality of life
Patient as: EORTC QLQ - H&N35

Patienter fortæller undertiden, at de har følgende symptomer eller problemer. Anfør venligst, i hvilken omfang De har haft disse symptomer eller problemer inden for den forlobne uge. Besvar spørgsmålene ved at sætte en ring omkring det tal, som passer bedst til Dem.

<table>
<thead>
<tr>
<th>I den forlobne uge:</th>
<th>Slet likke</th>
<th>Lidt</th>
<th>En del</th>
<th>Meget</th>
</tr>
</thead>
<tbody>
<tr>
<td>31. Har du haft smerter i munden?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>32. Har du haft smerter i kneben?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>33. Har du været som i munden?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>34. Har du haft ondt i halsen?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>35. Har du haft svært ved at synke væske?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>36. Har du haft svært ved at synke pureret mad?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>37. Har du haft svært ved at synke fast føde?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>38. Har de fået det galt i halsen, når de har sunket noget?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>39. Har du haft problemer med tenderne?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>40. Har du haft svært ved at åbne munden helt?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>41. Har De været tør i munden?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>42. Har dit spyt virket klevende?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>43. Har du haft problemer med hættesanser?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>44. Har De haft problemer med Deres smagssans?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>45. Har du hostet?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>46. Har du været hæs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>47. Har De følt Dem syg?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>48. Har dit udseende generet dig?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Gå venligst videre til næste side
Morbidity measures

- PHYSICAL FUNCTION
- SYMPTOMS
- OVERALL FUNCTION
- QUALITY OF LIFE

Increasing specificity
Increasing patient relevance
Factors important for HN late morbidity

- Dose
- Volume
- Fractionation
- Treatment time (acceleration)
- Chemotherapy
- Smoking
- Co-morbidity, performance status
Dysphagia

Functional Endoscopic Evaluation of Swallowing (FEES)
Functional Endoscopic Evaluation of Swallowing (FEES)
Functional Endoscopic Evaluation of Swallowing (FEES)
Swallowing problems are frequent

Jensen et al - 34 HN patients

- Reduced sensitivity: 94%
- Residues: 88%
- Penetration: 59%
- Aspiration: 18%
Can we predict?

Aspiration Risk Index

Dose effect
Median dose (Gy)
supraglottis
20 40 60 80

Proportion with aspiration risk index > median
0.0 0.2 0.4 0.6 0.8 1.0

\[ p = 0.034 \]

\[ \frac{0}{6} \quad \frac{3}{6} \quad \frac{3}{6} \quad \frac{5}{6} \]

Can we prevent?
- ongoing DAHANCA study with preventive physiotherapy
Xerostomia
Xerostomia

- C-Methionine PET
Xerostomia

• Consequences
  – Severe caries (acid neutralization)
  – Eating problems
    • Swallowing and taste
  – Speaking problems
  – Sleep

• Interventions
  – Parotic protective radiotherapy
  – Artificial salivia
  – Frequent dental care
  – Pharmacological (parasympatathomimetics)
Planning of radiotherapy
Dynamic IMRT - sliding windows
Intensity modulated radiotherapy (IMRT)

Aarhus University Hospital
RTOG Subjective Salivary Gland toxicity ≥G2*

Time post radiotherapy

<table>
<thead>
<tr>
<th>Time</th>
<th>CRT</th>
<th>IMRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>78</td>
<td>56</td>
</tr>
<tr>
<td>6 months</td>
<td>83</td>
<td>47</td>
</tr>
<tr>
<td>12 months</td>
<td>65</td>
<td>38</td>
</tr>
<tr>
<td>18 months</td>
<td>76</td>
<td>23</td>
</tr>
<tr>
<td>24 months</td>
<td>75</td>
<td>19</td>
</tr>
</tbody>
</table>

p-values:
- p=0.04
- p=0.001
- p=0.04
- p<0.001
- p<0.001

n:
- CRT: 41, 36, 34, 25, 24
- IMRT: 45, 45, 39, 35, 32

*Nutting et al. ESTRO 2010

*Moderate or complete dryness of mouth, poor or no response on stimulation
Change in Global QL from Baseline

Time since RT  | 2 wks  | 3 mths  | 6 mths  | 12 mths | 18 mths | 24 mths
--- | --- | --- | --- | --- | --- | ---
Difference (IMRT – CRT) | -1.8 | -4.8 | -3.1 | 1.9 | 3.5 | 11.1

Nutting et al. ESTRO 2010
Morbidity measures

- PHYSICAL FUNCTION
- SYMPTOMS
- OVERALL FUNCTION
- QUALITY OF LIFE

Increasing specificity
Increasing patient relevance
other problems
HEAD and NECK CARCINOMA

Primary loco-regional control and survival in 15,146 patients

- Local control: 10,008 pts (92%)
- Local Failure: 5,138 pts (68%)

Primary loco-regional control vs survival in 15,146 patients

HEAD and NECK CARCINOMA

- 14% survival
- 68% local control

Co-morbidity

Excess death due to co-morbidity and new primary cancer increase with age and limits the benefit of new therapeutic interventions

Produced by during coffee break at head and neck cancer meeting

Dead H&N cancer

All deaths

DAHANCA.dk
Age vs Comorbidity (Charlson scale)

DAHANCA database 2008+ (527 pts)

AGE in YEARS

PATIENTS WITH COMORBIDITY (%)

Charlson 1
Charlson 2+

< 50
22%
1

51-60
25%
1

61-70
43%
1

71+
58%
1

DAHANCA.dk
A new cancer type dominates head and neck cancer

Incidence of oropharyngeal and laryngeal carcinoma

Denmark 1977-2007

DAHANCA database

Lassen, Radiother Oncol, 2010
Influence of HPV (p16 pos) on outcome after radiotherapy of HNSCC

HPV infection is the strongest prognostic factor in HN cancer - and because these patients are younger may they indirectly change the age relationship - We are simply getting a new group of 50-60 year old patients with a very good prognosis.
- The need for rehabilitation in head and neck cancer - conclusion

- The need for rehabilitation is strongly linked with treatment related morbidity.
- Thus active modification and intervention may reduce the demand for rehabilitation.
- The patient cohort is likely to change towards younger and more fit persons with better performance status (fewer problems), and a better prognosis (HPV pos).
Important research areas

• Measures of morbidity closer related to therapeutic induced damage (specificity)
• Understanding the consequences for the patient (relevance)
• Implement and investigate intervention measures
• Measure the overall strain to the patient