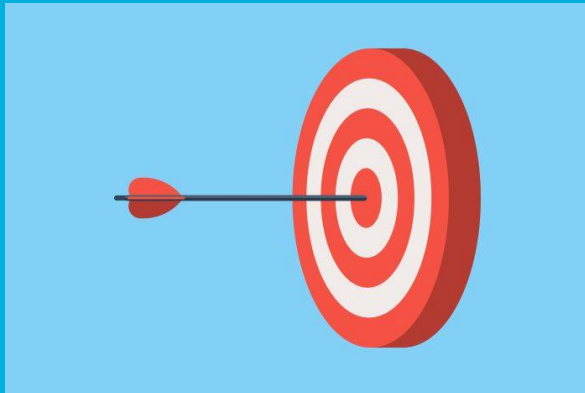


# Challenges and Needs in Head and Neck Oncological Surgery



Robert Takes

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# Head and Neck Cancer

- Fast growing tumors in vulnerable area of human body
- High rate of regional lymph node metastasis
- If primary treatment insufficient: adjuvant treatment

- Survival



- Functioning



- Quality of life



- Higher costs

- Sustainability



Health Status

- Poor
- Average
- Excellent



---

# First Time Right



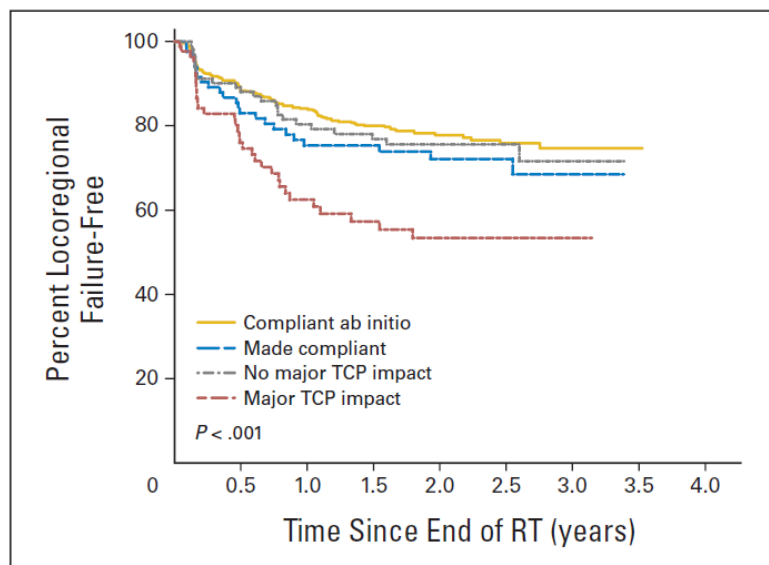
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# Value-based health care



## Critical Impact of Radiotherapy Protocol Compliance and Quality in the Treatment of Advanced Head and Neck Cancer: Results From TROG 02.02

Lester J. Peters, Brian O'Sullivan, Jordi Giralt, Thomas J. Fitzgerald, Andy Trotti, Jacques Bernier, Jean Bourhis, Kally Yuen, Richard Fisher, and Danny Rischin



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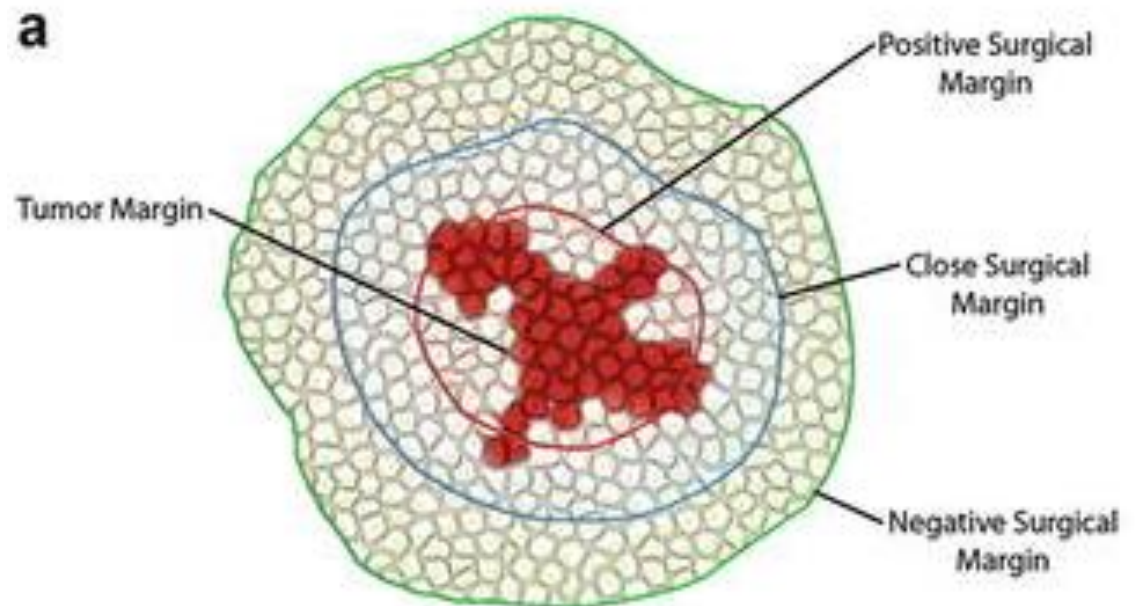
# Conclusion

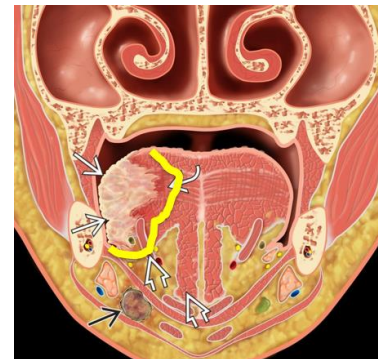
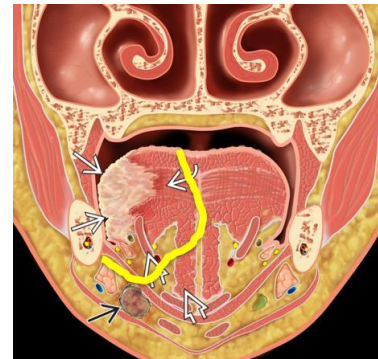
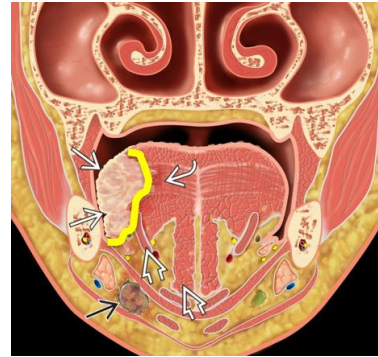
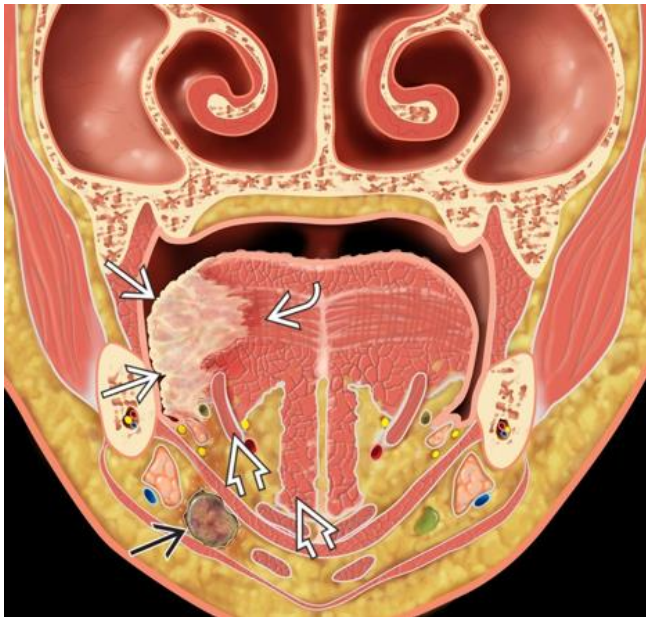
- “There are several important lessons regarding radiotherapy quality that should be learned from this trial. **The first is that the impact of poor radiotherapy can greatly exceed the anticipated benefit of concurrent chemotherapy.**”
- “In the overall context of head and neck cancer treatment in the community, these results strongly reinforce the importance of doing well what we already know. **It is sobering to note that the value of good radiotherapy is substantially greater than the incremental gains that have been achieved with new drugs and/or biologicals.**”
- “Although the existence of such detriments is generally recognized, **the magnitude detected (ie, a 20% reduction in the absolute 2-year survival rate) is astounding.**”

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# Head and Neck Surgery

- Primary tumor: adequacy of resection margins determines need for adjuvant treatment
- <1mm
- 1-5 mm
- >5 mm

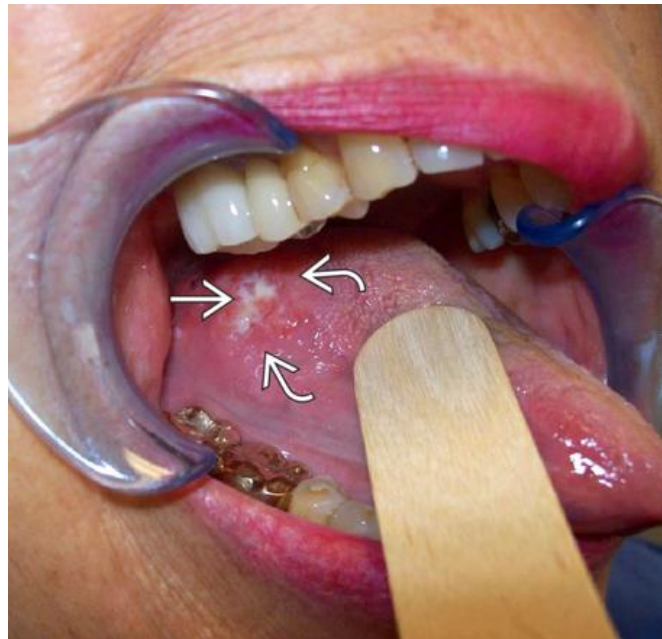






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# Head and Neck Surgery



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# Head and neck Surgery

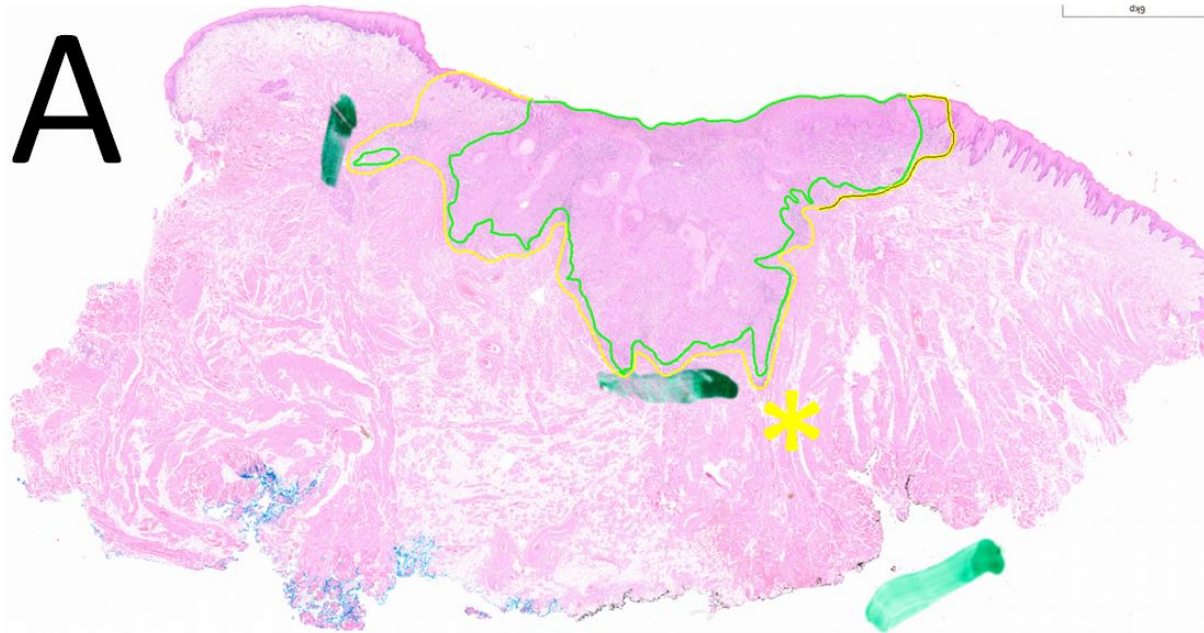
- “Translation” of pre-operative imaging
- Visual and tactile / palpation



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# Histopathology and tumor board

- > Days after surgery



## Resection margins in oral cancer surgery: Room for improvement

Roeland W.H. Smits, MD,<sup>1,2</sup> Senada Koljenović, MD, PhD,<sup>2,3\*</sup> Jose A. Hardillo, MD, PhD,<sup>1</sup> Ivo ten Hove, MD,<sup>1,2,4</sup> Cees A. Meeuwis, MD, PhD,<sup>1</sup> Aniel Sewnaik, MD, PhD,<sup>1</sup> Emilie A.C. Dronkers, MD,<sup>1</sup> Tom C. Bakker Schut, MSc, PhD,<sup>2</sup> Ton P.M. Langeveld, MD, PhD,<sup>5</sup> Jan Molenaar, BSc,<sup>6</sup> V. Noordhoek Hegt, MD, PhD,<sup>3</sup> Gerwin J. Puppels, MSc, PhD,<sup>2</sup> Robert J. Baatenburg de Jong, MD, PhD<sup>1</sup>

<sup>1</sup>Department of Otorhinolaryngology and Head and Neck Surgery, Erasmus University Medical Center, Medical Center Rotterdam, Rotterdam, The Netherlands, <sup>2</sup>Center for Optical Diagnostics and Therapy, Department of Dermatology, Erasmus University Medical Center, University Medical Center Rotterdam, Rotterdam, The Netherlands, <sup>3</sup>Department of Pathology, Erasmus University Medical Center, University Medical Center Rotterdam, Rotterdam, The Netherlands, <sup>4</sup>Department of Oral and Maxillofacial surgery, Erasmus University Medical Center, University Medical Center Rotterdam, Rotterdam, The Netherlands, <sup>5</sup>Department of Otorhinolaryngology and Head and Neck Surgery, Leiden University, Medical Center, Leiden, The Netherlands, <sup>6</sup>Department of Oncology Documentation, Leiden University Medical Center, Leiden, The Netherlands.

*Accepted 13 April 2015*

*Published online 15 June 2015 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/hed.24075*

# Resection margins

Margins	no. (%)
Positive <1 mm	160 (22)
Narrow 1-4 mm	450 (61)
Adequate ≥5 mm	125 (17)

Erasmus MC Margins	n = 174 (%)
Positive <1 mm	43
Narrow 1-5 mm	42
Adequate >5 mm	15

LUMC Margins	n = 117 (%)
Positive <1 mm	40
Narrow 1-5 mm	45
Adequate >5 mm	15

# Resection margins

Margins	no. (%)
Positive <1 mm	160 (22)
Narrow 1-4 mm	450 (61)
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Positive <1 mm	40
Narrow 1-5 mm	45
Adequate >5 mm	15

# Distributie resectiemarges

Resectiemarges	Frequentie – no. (%)
Positieve marge, <1 mm	160 (22)
Krappe marge, 1-4 mm	450 (61)
Vrije marge, ≥5 mm	125 (17)

Erasmus MC Resectiemarges	n = 174 Frequentie – (%)
Positieve marge, <1 mm	43
Krappe marge, 1-5 mm	42
Vrije marge, >5 mm	15

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Positieve marge, <1 mm	40
Krappe marge, 1-5 mm	45
Vrije marge, >5 mm	15

# Distributie resectiemarges

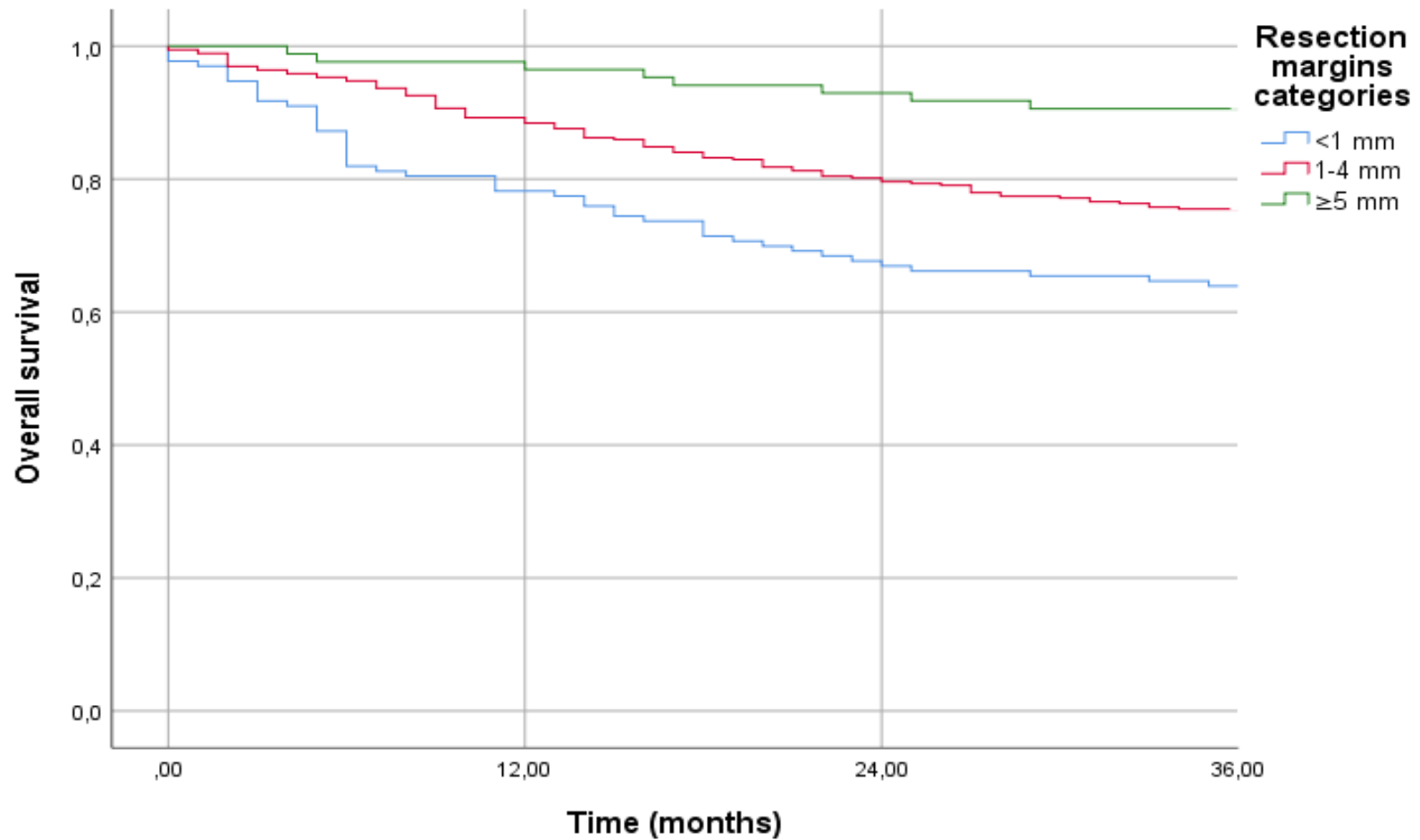
Resectiemarges	Frequentie – no. (%)
Positieve marge, <1 mm	160 (22)
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Positieve marge, <1 mm	40
Krappe marge, 1-5 mm	45
Vrije marge, >5 mm	15



# 3-year overall survival

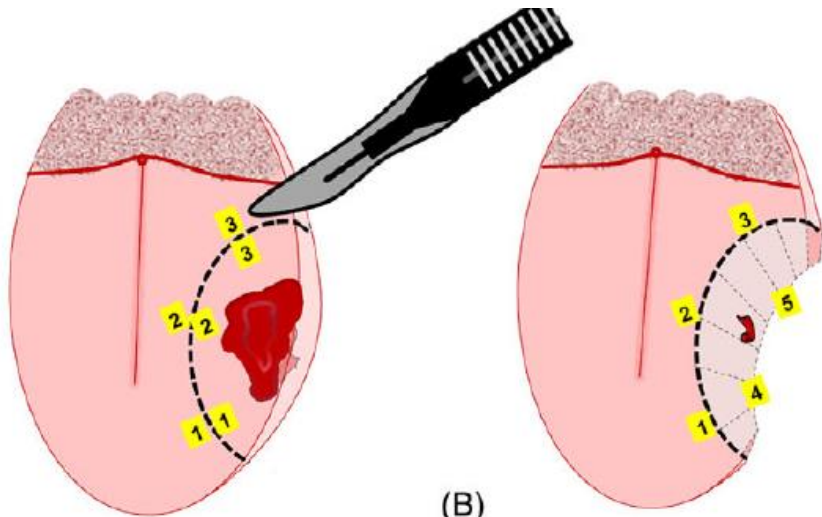


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# Improvement

- Intra Operative Assessment of Resection Margins (IOARM)
- Optical and Image Guided Surgery (OIGS)



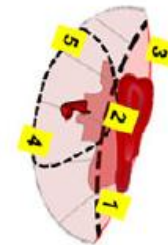


(A)

Application of the tags in a pair-wise manner.

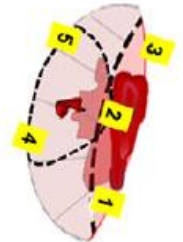
(B)

Wound bed with tags.



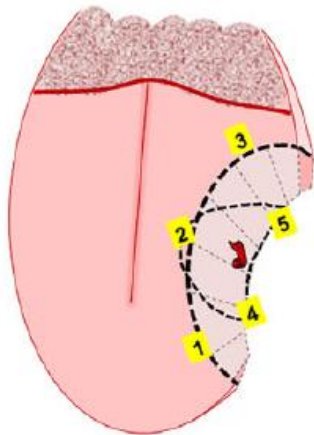
(C)

Specimen with corresponding tags.



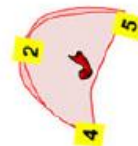
(D)

Intra-operative specimen-driven assessment: inadequate margin between tag 2-4-5 with thickness of 2mm.



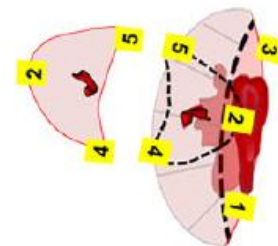
(E)

Relocation of inadequate margin in the wound bed. (tag 2-4-5 as indicated by the pathologist)



(F)

Additional resection enclosing the tags and thickness as indicated by pathologist

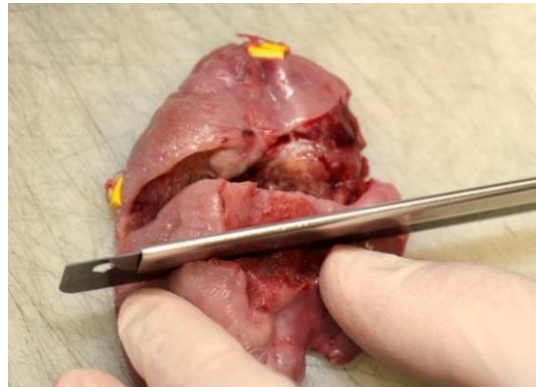
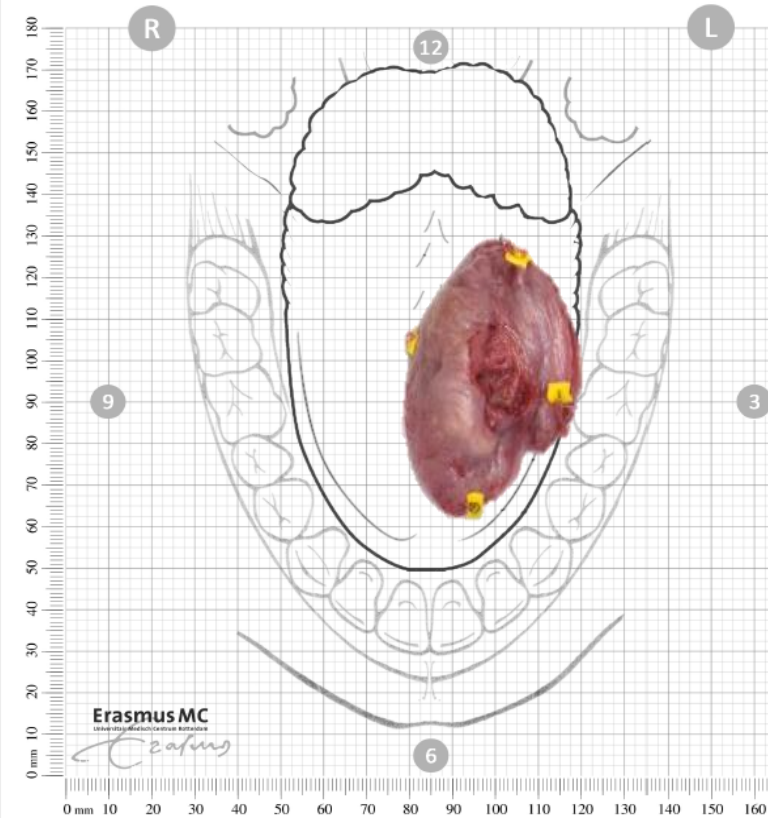


(G)

Correlation of additional resection with main resection specimen.

# Intra-operative assessment

Tongue - superior

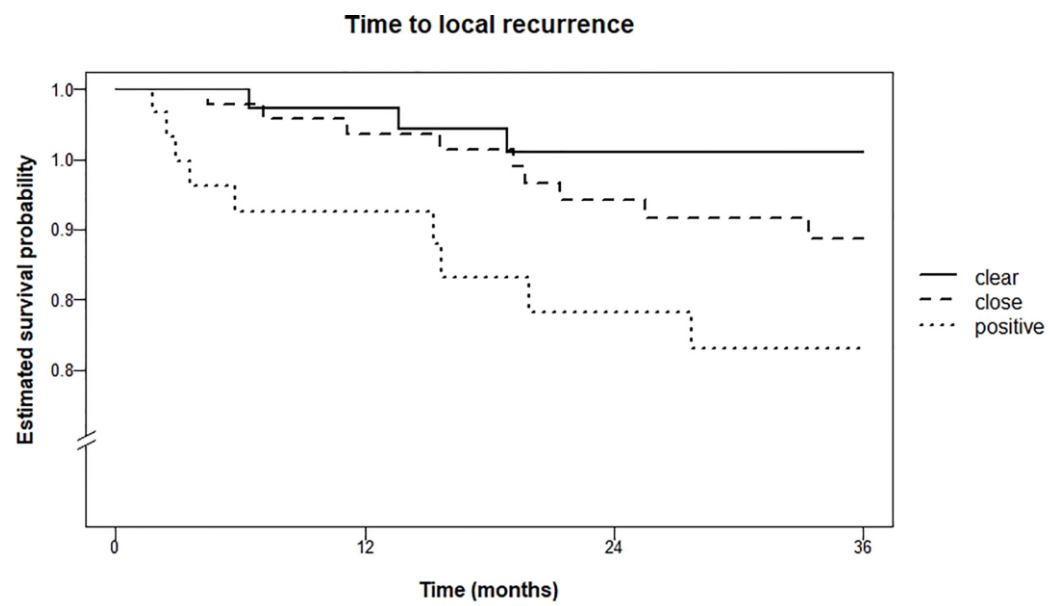


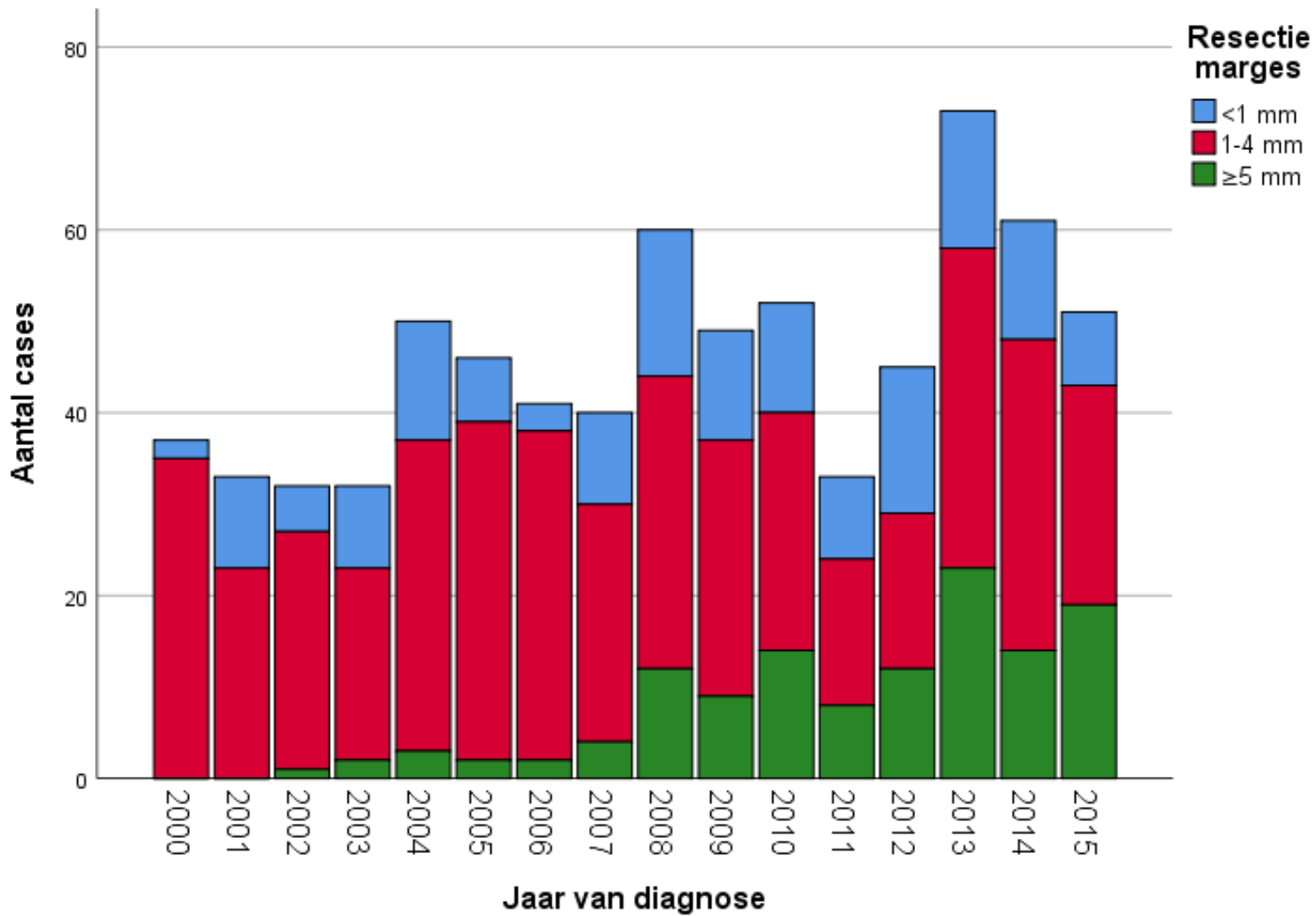


# Intraoperative Assessment of the Resection Specimen Facilitates Achievement of Adequate Margins in Oral Carcinoma

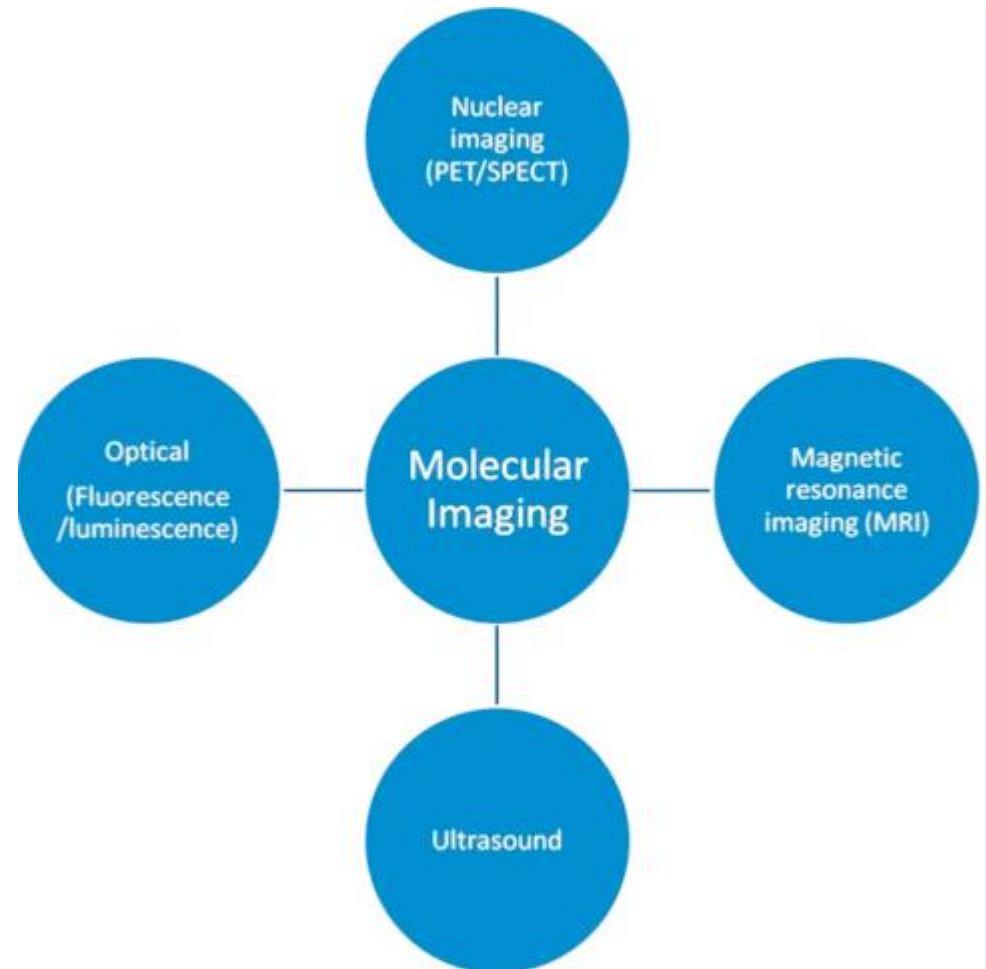
*Roeland W. H. Smits<sup>1,2\*</sup>, Cornelia G. F. van Lanschoot<sup>1,2</sup>, Yassine Aaboubout<sup>3</sup>, Maria de Ridder<sup>4</sup>, Vincent Noordhoek Hegt<sup>3</sup>, Elisa M. Barroso<sup>4,5</sup>, Cees A. Meeuwis<sup>1</sup>, Aniel Sewnaik<sup>1</sup>, Jose A. Hardillo<sup>1</sup>, Dominiek Monserez<sup>1</sup>, Stijn Keereweer<sup>1</sup>, Hetty Mast<sup>5</sup>, Ivo Ten Hove<sup>5</sup>, Tom C. Bakker Schut<sup>2</sup>, Robert J. Baatenburg de Jong<sup>1</sup>, Gerwin J. Puppels<sup>2</sup> and Senada Koljenović<sup>3</sup>*

	None		Defect-driven		Specimen-driven	
	2010–2012	2013–2017	2010–2012	2013–2017	2010–2012	2013–2017
-adequate	n = 150 24 (16%)	n = 95 16 (17%)	n = 16 2 (12.5%)	n = 65 15 (23%)	n = 8 0 (0%)	n = 81 47 (58%)
-close	62 (41%)	49 (52%)	6 (37.5%)	31 (48%)	3 (37.5%)	21 (26%)
-tumor-positive	64 (43%)	30 (31%)	8 (50%)	19 (29%)	5 (62.5%)	13 (16%)





# Techniques



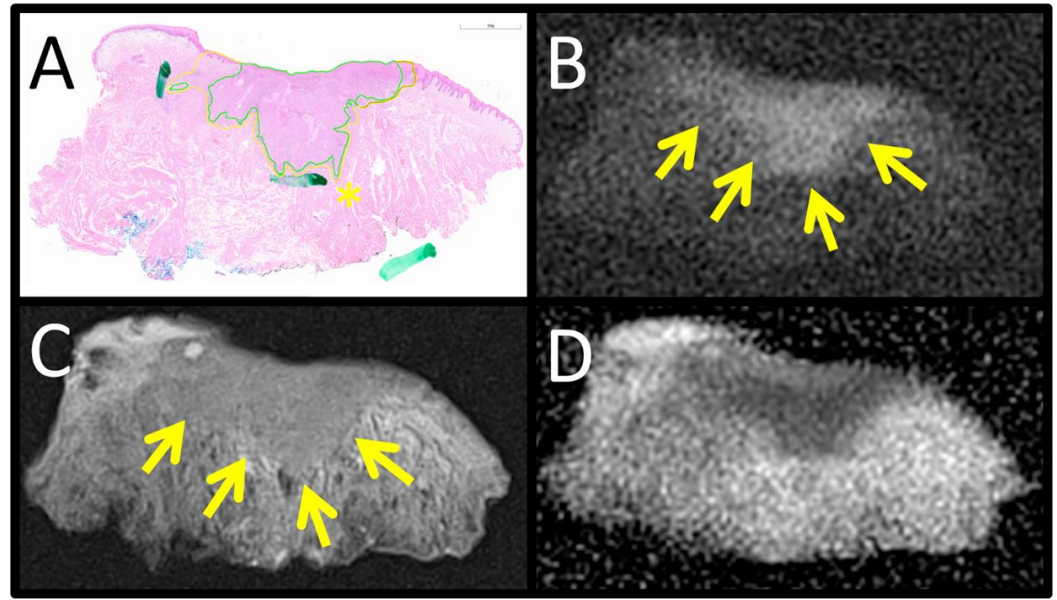


# Ex vivo MRI

- Ex vivo MRI
  - Pilot 7T
  - Pilot 3T

Int J CARS (2017) 12:821–828  
DOI 10.1007/s11548-017-1524-6

ORIGINAL ARTICLE

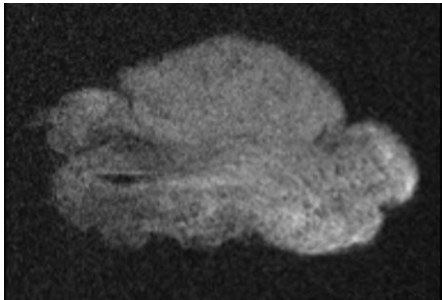


## Evaluation of tongue squamous cell carcinoma resection margins using ex-vivo MR

Stefan C. A. Steens<sup>1</sup> · Elise M. Bekers<sup>2</sup> · Willem L. J. Weijs<sup>3</sup> · Geert J. S. Litjens<sup>2</sup> ·  
Andor Veltien<sup>1</sup> · Arie Maat<sup>2</sup> · Guido B. van den Broek<sup>4</sup> ·  
Jeroen A. W. M. van der Laak<sup>2</sup> · Jürgen J. Fütterer<sup>1</sup> ·  
Christina A. Hulsbergen van der Kaa<sup>2</sup> · Matthias A. W. Merks<sup>3</sup> · Robert P. Takes<sup>4</sup>

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# Ex vivo MRI





Received: 21 November 2019 | Revised: 29 January 2020 | Accepted: 20 February 2020

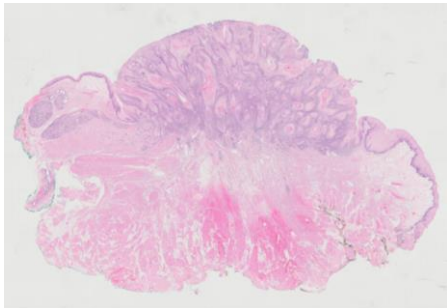
DOI: 10.1002/hed.26125

## ORIGINAL ARTICLE

WILEY

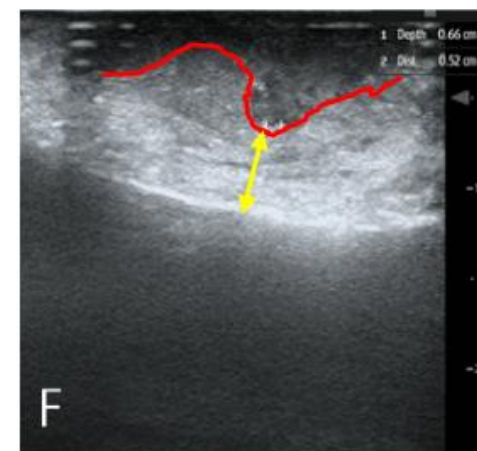
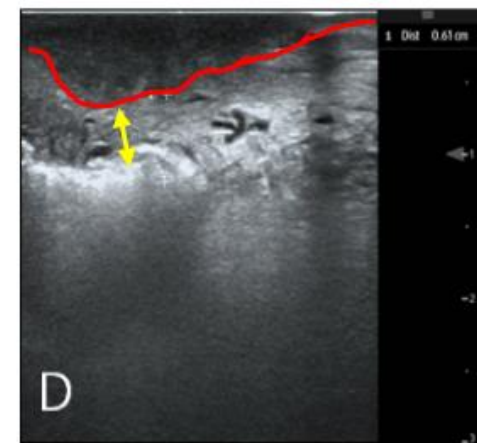
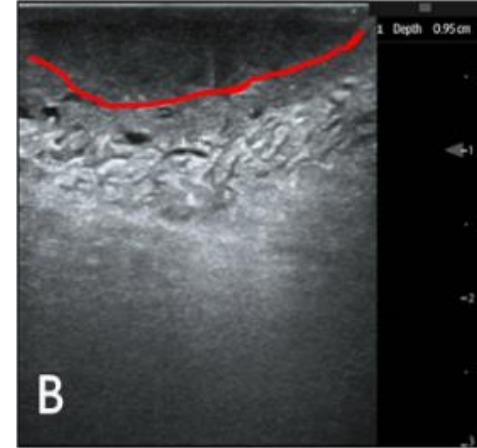
### **Assessment of surgical tumor-free resection margins in fresh squamous-cell carcinoma resection specimens of the tongue using a clinical MRI system**

Jan Heidkamp MS<sup>1</sup>  | Willem L. J. Weijs MD<sup>2</sup> |  
Adriana C. H. van Engen-van Grunsven MD, PhD<sup>3</sup> | Ilse de Laak-de Vries BS<sup>3</sup> |  
Marnix C. Maas PhD<sup>1</sup> | Maroeska M. Rovers PhD<sup>4,5</sup> |  
Jurgen J. Fütterer MD, PhD<sup>1</sup> | Stefan C. A. Steens MD; PhD<sup>1</sup> |  
Robert P. Takes MD, PhD<sup>6</sup> 



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# Ultrasound





Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

## Oral Oncology

journal homepage: [www.elsevier.com/locate/oraloncology](http://www.elsevier.com/locate/oraloncology)



Feasibility study of ultrasound-guided resection of tongue cancer with immediate specimen examination to improve margin control – Comparison with conventional treatment

[Klijs J. de Koning<sup>a,b</sup>](#), [Sjors A. Koppes<sup>c</sup>](#), [Remco de Bree<sup>a</sup>](#), [Jan Willem Dankbaar<sup>d</sup>](#),  
[Stefan M. Willems<sup>c,e</sup>](#), [Robert J.J. van Es<sup>a,b</sup>](#), [Rob Noorlag<sup>a,b,\\*</sup>](#)

Histopathological margins found in US and conventional cohorts.

	<i>US cohort (n = 10)</i>	<i>Conventional cohort (n = 91)</i>	<i>P-value</i>
<i>Margin status (n)</i>			
Free (%)	7 (70)	15 (17)	0.005 <sup>a</sup>
Close (%)	2 (20)	67 (74)	
Positive (%)	1 (10)	9 (10)	

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# Raman



# Raman spectroscopy



## Analyst



PAPER

[View Article Online](#)  
[View Journal](#) | [View Issue](#)



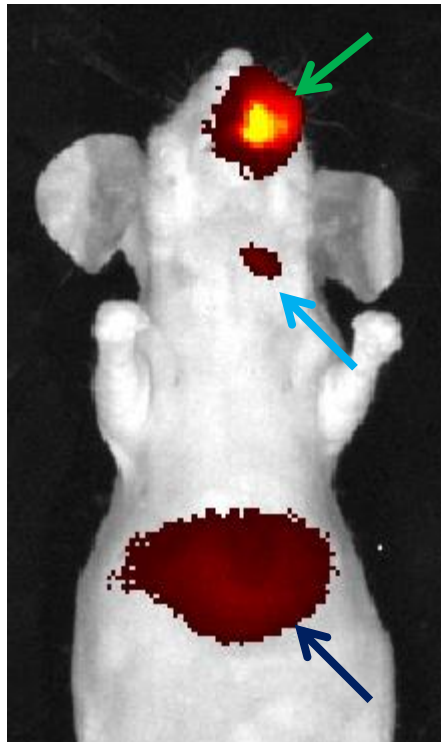
Cite this: *Analyst*, 2018, **143**, 4090

## Raman spectroscopic analysis of the molecular composition of oral cavity squamous cell carcinoma and healthy tongue tissue†

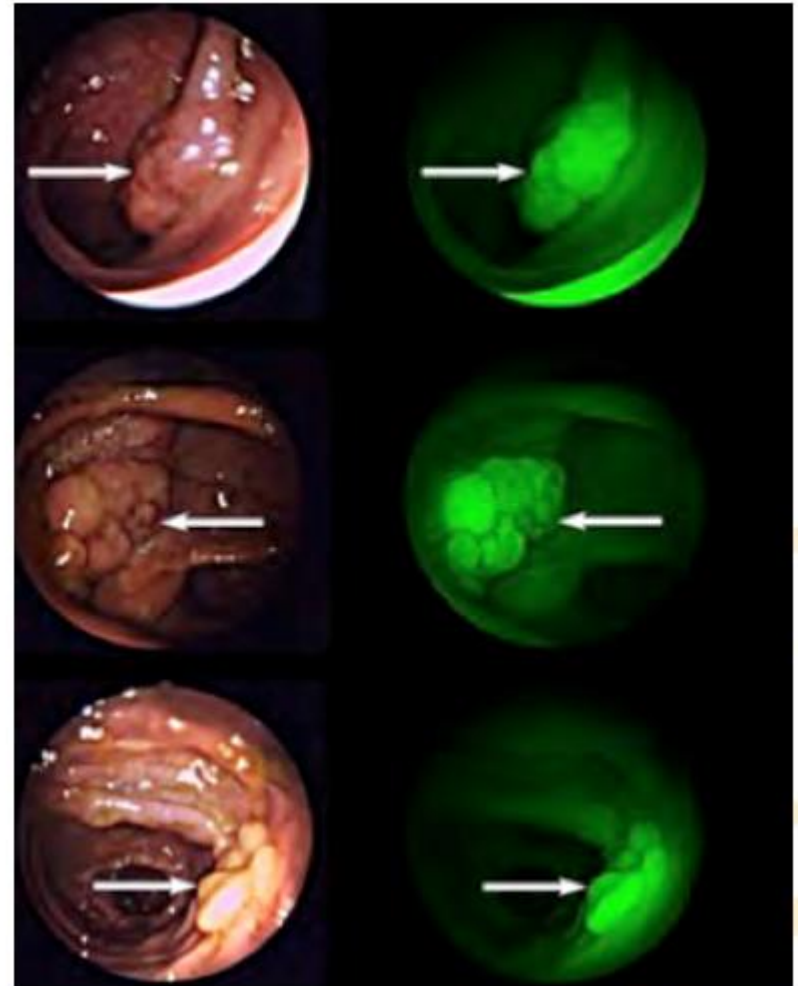
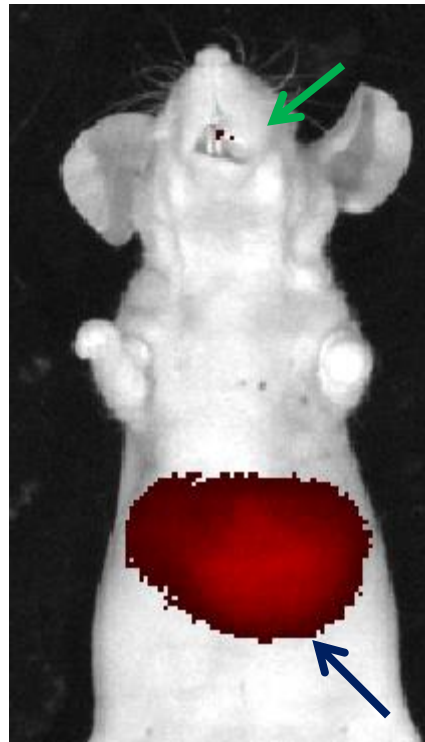
F. L. J. Cals, <sup>a,b</sup> T. C. Bakker Schut,<sup>\*b</sup> P. J. Caspers,<sup>b</sup> R. J. Baatenburg de Jong, <sup>a</sup>  
S. Koljenović<sup>c</sup> and G. J. Puppels<sup>b</sup>

# NIR-fluorescence

Bivatuzumab

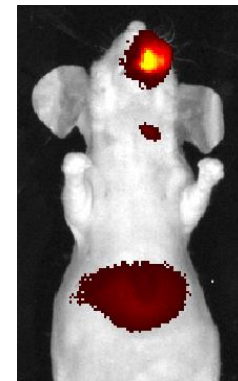
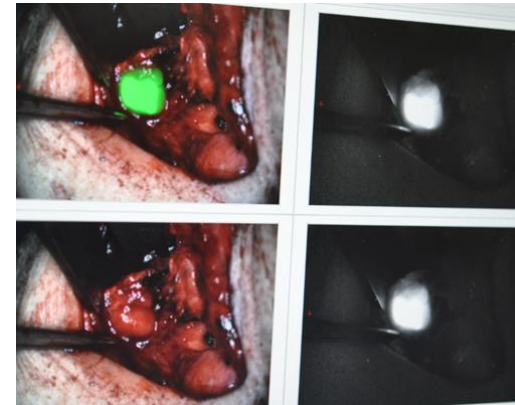


IgG1



# Fluorescence-guided surgery

- Fluorescence
  - Preclinical research
  - Identification clinical grade antibodies
  - Clinical implementation



[www.nature.com/scientificreports](http://www.nature.com/scientificreports)

## SCIENTIFIC REPORTS

OPEN

### Targeting CD44v6 for fluorescence-guided surgery in head and neck squamous cell carcinoma

Received: 16 October 2017

Accepted: 8 June 2018


Published online: 11 July 2018

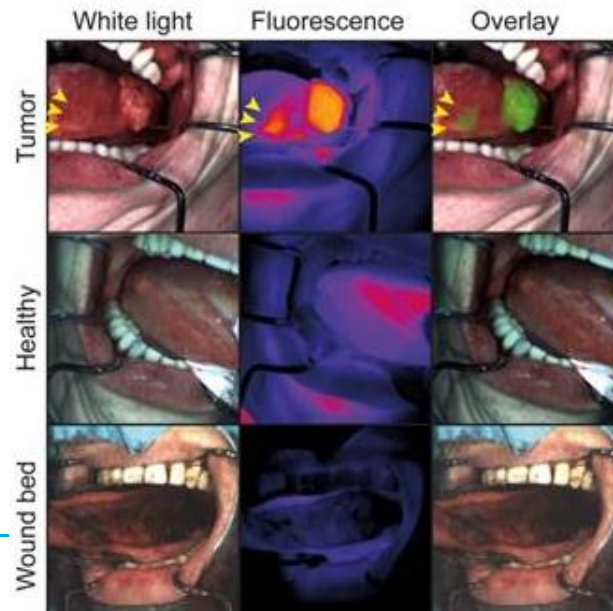
Julia Odenthal<sup>1,2</sup>, Mark Rijpkema<sup>3</sup>, Desirée Bos<sup>3</sup>, Esther Wagena<sup>2</sup>, Huib Croes<sup>2</sup>, Reidar Grenman<sup>4</sup>, Otto Boerman<sup>3</sup>, Robert Takes<sup>1</sup> & Peter Friedl<sup>2,5,6</sup>



Research Paper

# Fluorescence-guided imaging for resection margin evaluation in head and neck cancer patients using cetuximab-800CW: A quantitative dose-escalation study

Floris Jan Voskuil<sup>1\*</sup>, Steven Jakob de Jongh<sup>2\*</sup>, Wouter Tjerk Rudolph Hooghiemstra<sup>2,3</sup>, Matthijs David Linsen<sup>2,3</sup>, Pieter Jan Steinkamp<sup>4</sup>, Sebastiaan Antonius Hendrik Johannes de Visscher<sup>1</sup>, Kees-Pieter Schepman<sup>1</sup>, Sjoerd Geert Elias<sup>5</sup>, Gert-Jan Meersma<sup>2</sup>, Pascal Klaas Christiaan Jonker<sup>4</sup>, Jan Johannes Doff<sup>6</sup>, Annelies Jorritsma-Smit<sup>3</sup>, Wouter Bastiaan Nagengast<sup>2</sup>, Bert van der Vegt<sup>6</sup>, Dominic James Robinson<sup>7</sup>, Gooitzen Michell van Dam<sup>4,8</sup>, Max Johannes Hendrikus Witjes<sup>1</sup>



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# PET-CT









Journal of  
*Clinical Medicine*

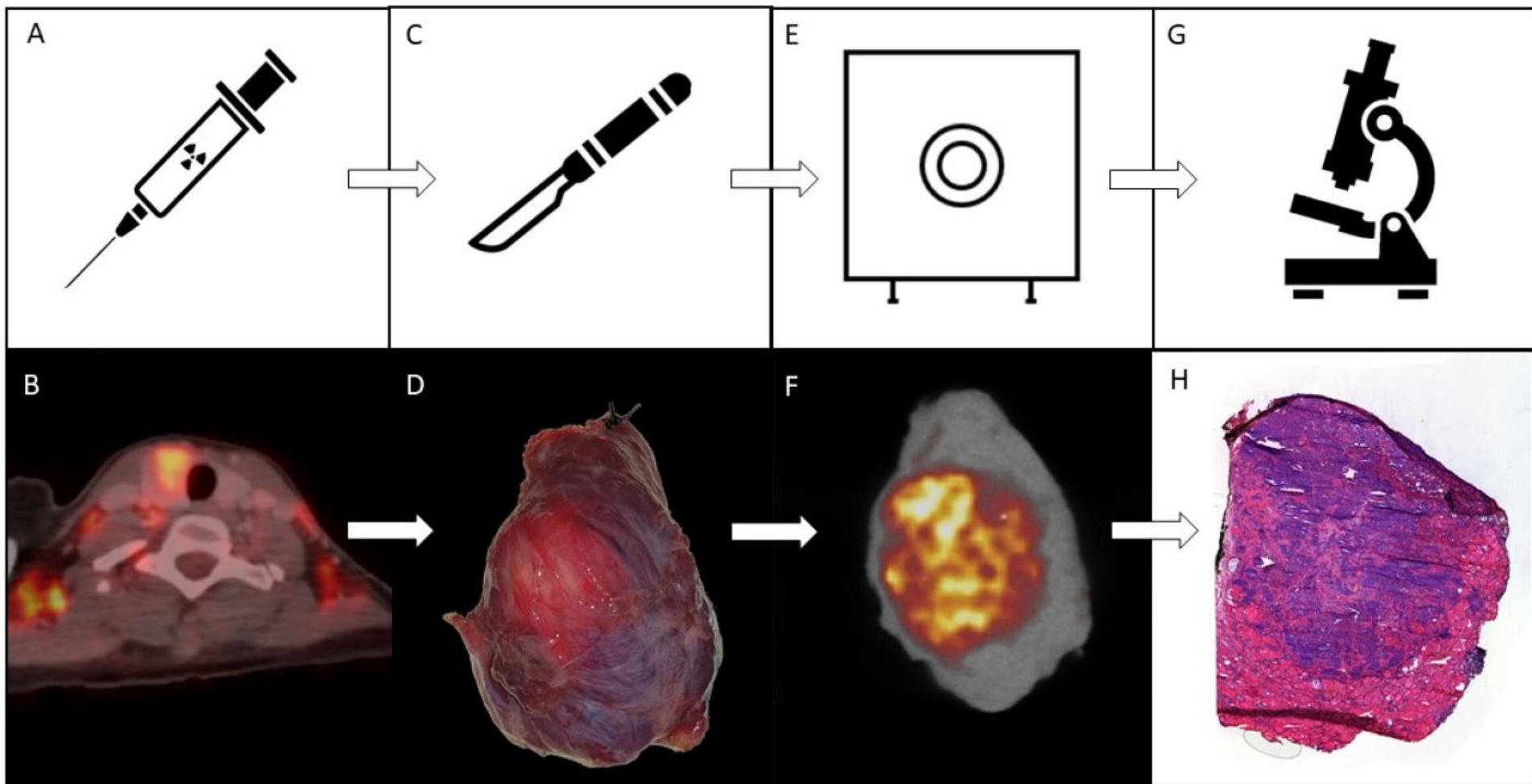
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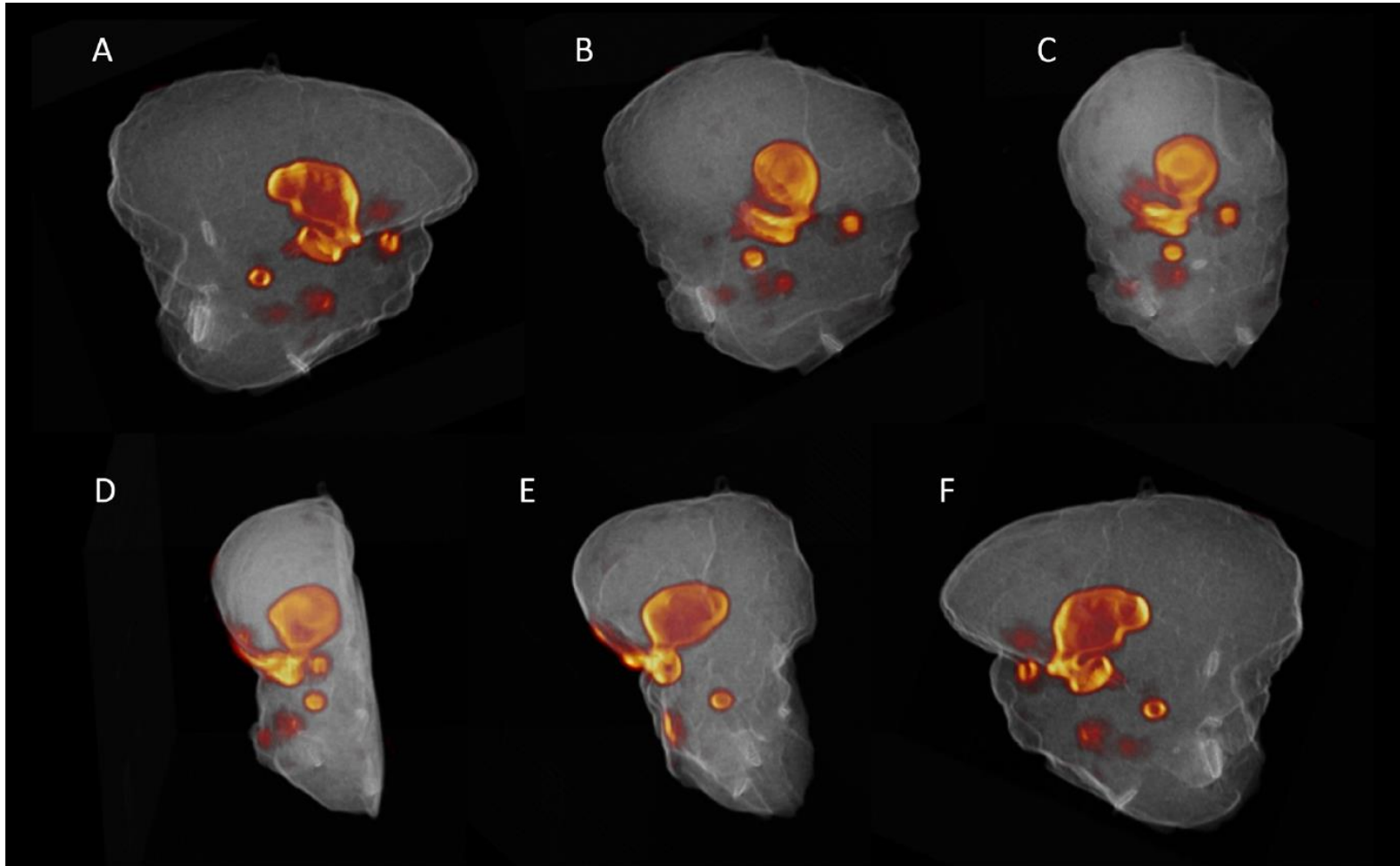


Article

## High-Resolution $^{18}\text{F}$ -FDG PET/CT for Assessing Three-Dimensional Intraoperative Margins Status in Malignancies of the Head and Neck, a Proof-of-Concept

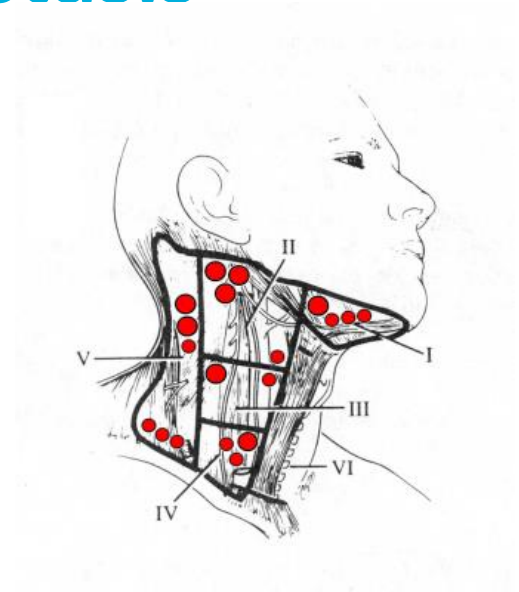
Jens M. Debacker <sup>1,2,3,4,\*</sup> , Vanessa Schelfhout <sup>4,5,6</sup>, Lieve Brochez <sup>1,4,7</sup> , David Creytens <sup>4,6,8</sup> ,  
Yves D'Asseler <sup>4,5,6</sup>, Philippe Deron <sup>1,2,4</sup>, Vincent Keereman <sup>9,10</sup>, Koen Van de Vijver <sup>4,6,8</sup> ,  
Christian Vanhove <sup>4,9,11</sup>  and Wouter Huvenne <sup>1,2,4</sup> 





# Regional lymph node metastasis

- High rate of regional metastasis
- Limitation in detection (size)

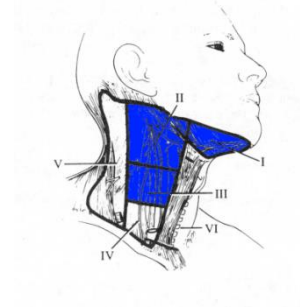
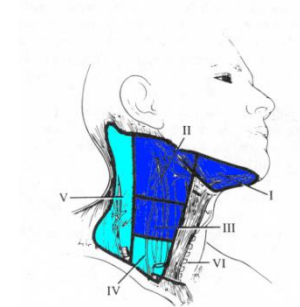


	<b>sensitivity</b>	<b>specificity</b>
Palpation	60-70%	60-70%
CT/MRI (cN0)	50-60%	75-85%
US + FNAC (cN0)	40-70%	100%

---

# Neck dissection

- cN+: (Modified) Radical neck dissection (ND I-V)
- cN0: Selective neck dissection (ND I-III)
- 80% overtreatment in patients without metastasis



# NECK TREATMENT AND SHOULDER MORBIDITY: STILL A CHALLENGE

Patrick J. Bradley, MB, BCh, BAO, DCH, MBA, FRCS (Ed, Eng, Ir), FHKCORL, FRCSLT (Hon), FRACS (Hon),<sup>1</sup> Alfio Ferlito, MD, DLO, DPath, FRCSEd *ad hominem*, FRCS (Eng, Glasg, Ir) *ad eundem*, FDSRCS *ad eundem*, FHKCORL, FRCPath, FASCP, IFCAP,<sup>2</sup> Carl E. Silver, MD,<sup>3</sup> Robert P. Takes, MD, PhD,<sup>4</sup> Julia A. Woolgar, FRCPath, PhD,<sup>5</sup> Primož Strojjan, MD,<sup>6</sup> Carlos Suárez, MD, PhD,<sup>7,8</sup> Hakan Coskun, MD,<sup>9</sup> Peter Zbären, MD,<sup>10</sup> Alessandra Rinaldo, MD, FRCSEd *ad hominem*, FRCS (Eng, Ir) *ad eundem*, FRCSGlasg<sup>2</sup>

Oral Oncology 122 (2021) 105510



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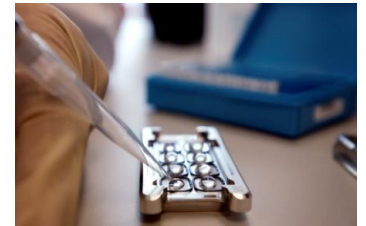
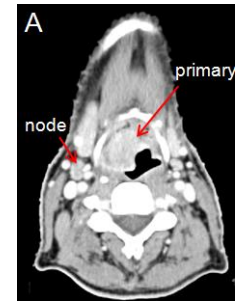
Effect of elective neck dissection versus sentinel lymph node biopsy on shoulder morbidity and health-related quality of life in patients with oral cavity cancer: A longitudinal comparative cohort study

Gerben van Hinte<sup>a,\*</sup>, Tolunay Sancak<sup>b</sup>, Willem L.J. Weijs<sup>b</sup>, Matthias A.W. Merx<sup>b,c</sup>,  
Ruud A. Leijendekkers<sup>a,e,f</sup>, Maria W.G. Nijhuis-van der Sanden<sup>a,d</sup>, Robert Takes<sup>f</sup>,  
Caroline M. Speksnijder<sup>b,g,h</sup>

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# Improvement

- Better diagnostics
  - Imaging
  - Predictors based on features primary tumor
    - Histology
    - “Biomarkers”
- Sentinel node procedure



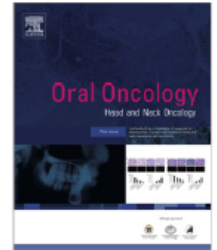




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## Oral Oncology

journal homepage: [www.elsevier.com/locate/oraloncology](http://www.elsevier.com/locate/oraloncology)



# Management of the N<sub>0</sub> neck in early stage oral squamous cell cancer: A modeling study of the cost-effectiveness



Tim M. Govers<sup>a,\*</sup>, Robert P. Takes<sup>b</sup>, Baris Karakullukcu<sup>c</sup>, Gerjon Hannink<sup>a</sup>, Matthias A.W. Merkx<sup>d</sup>,  
Janneke P.C. Grutters<sup>a,e</sup>, Maroeska M. Rovers<sup>a,e</sup>

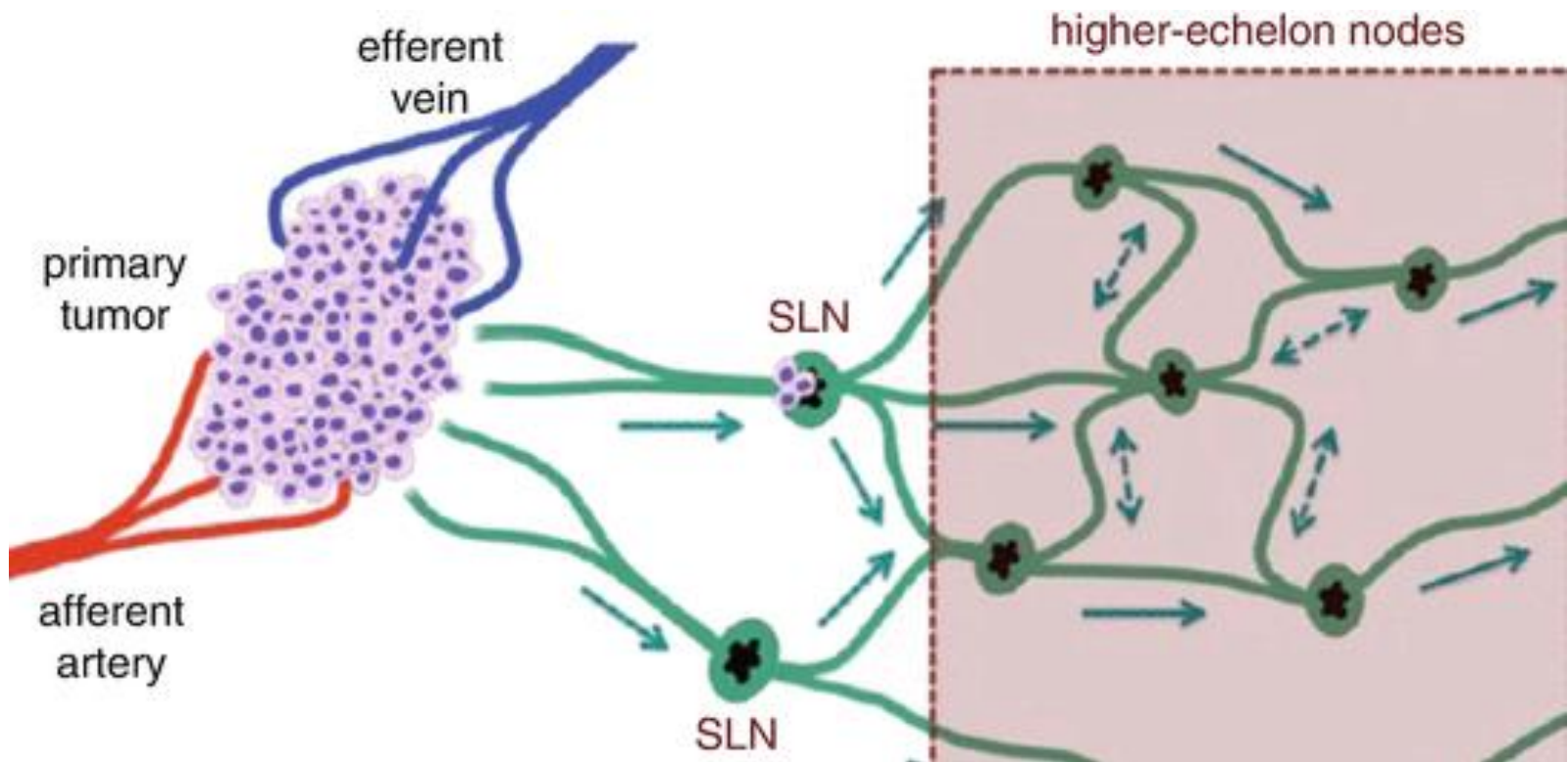
<sup>a</sup>Department of Operating Rooms, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

<sup>b</sup>Department of Otorhinolaryngology and Head and Neck Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

<sup>c</sup>Department of Head and Neck Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands

<sup>d</sup>Department of Oral and Maxillofacial Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

<sup>e</sup>Department of Health Evidence, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands



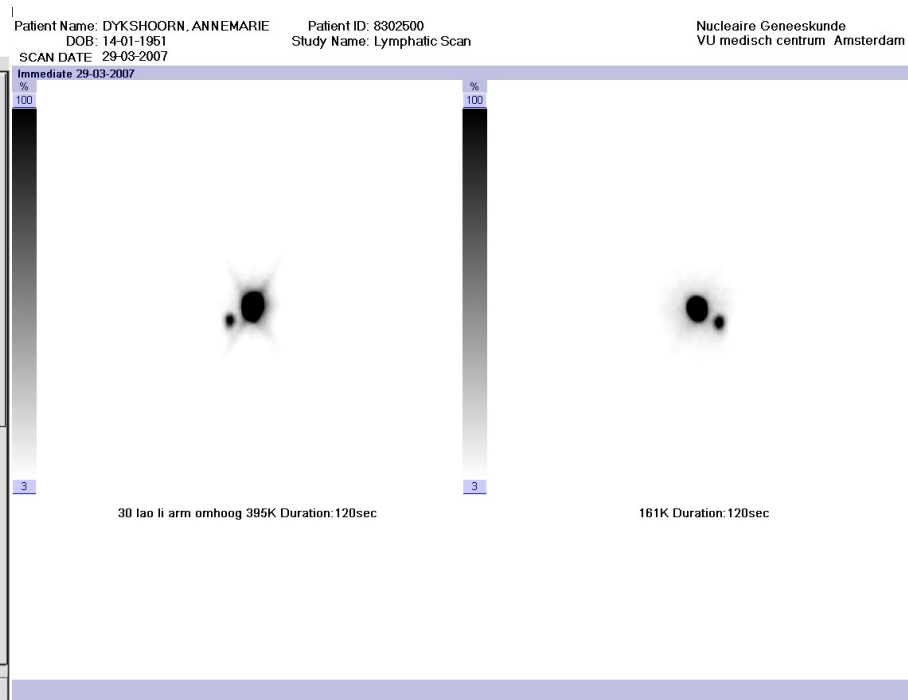
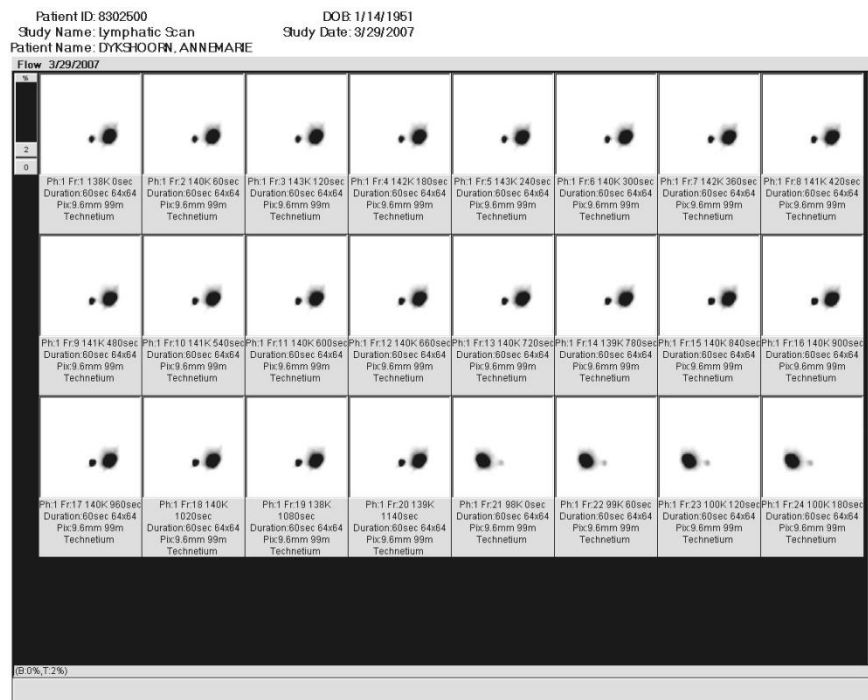
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# Pre-operative



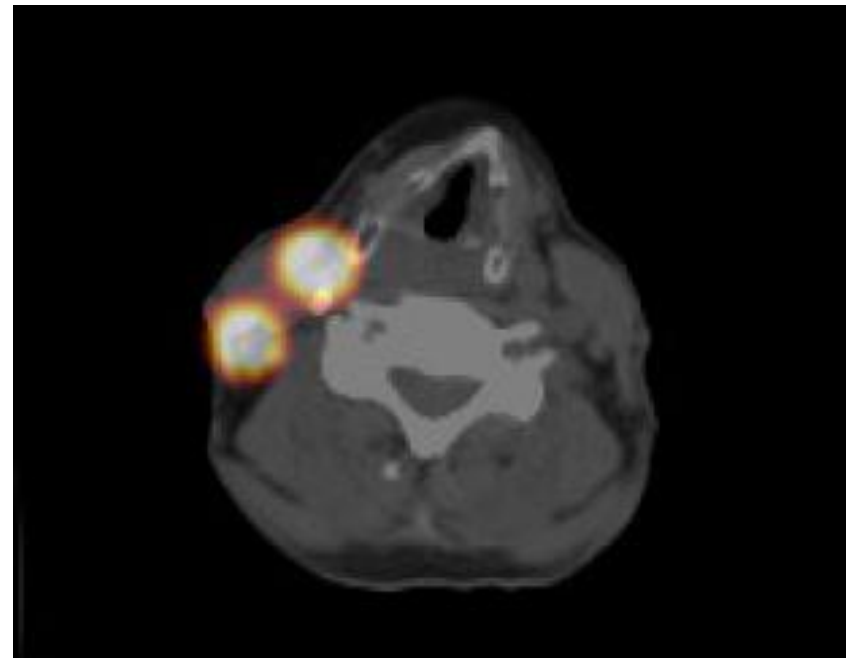
# Lymfoscintigraphy

- Dynamic and static



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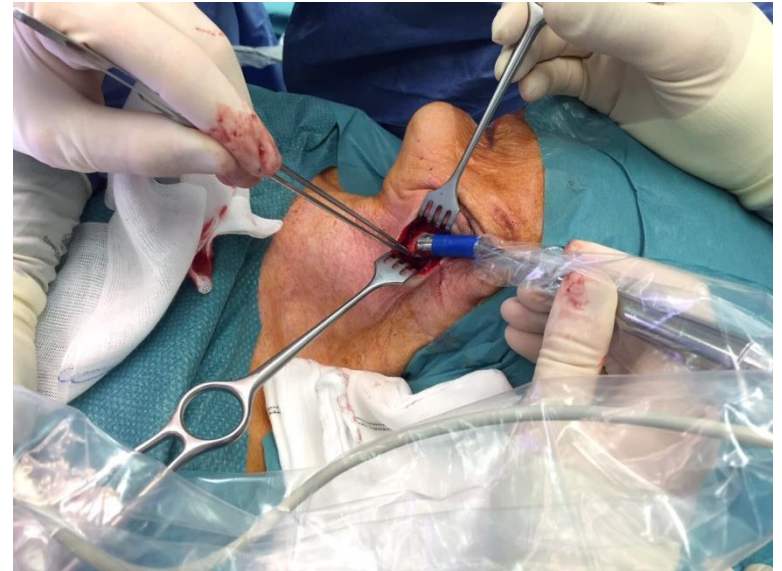
## SPECT-CT





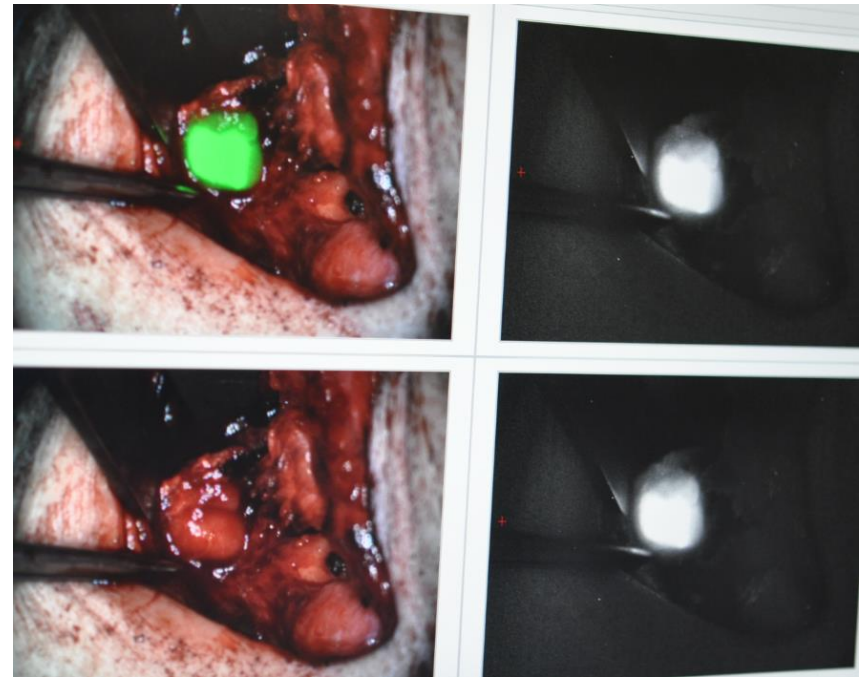
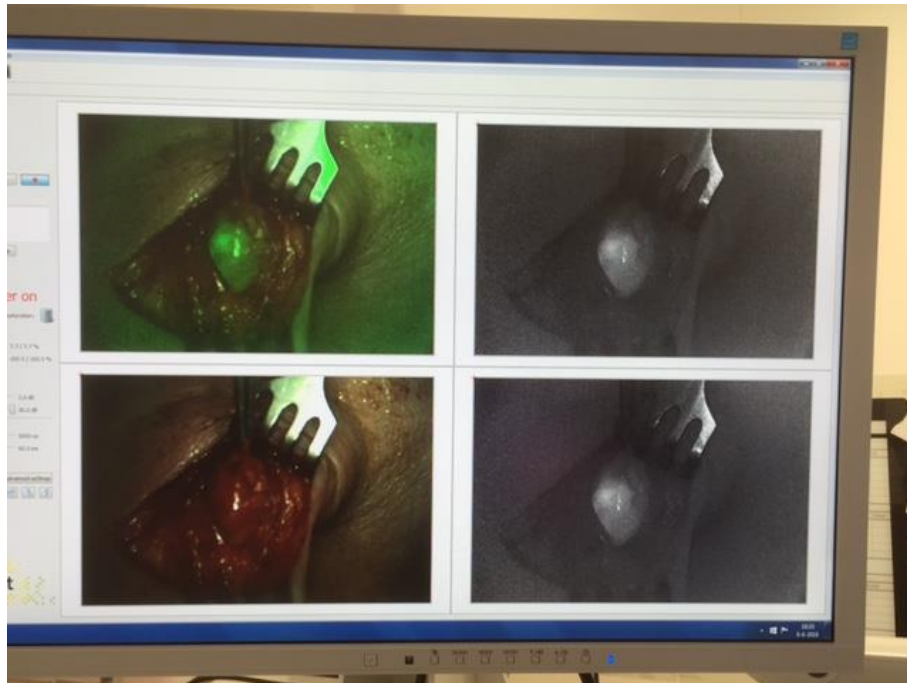
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# Intra-operative detection



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# Peroperative detection

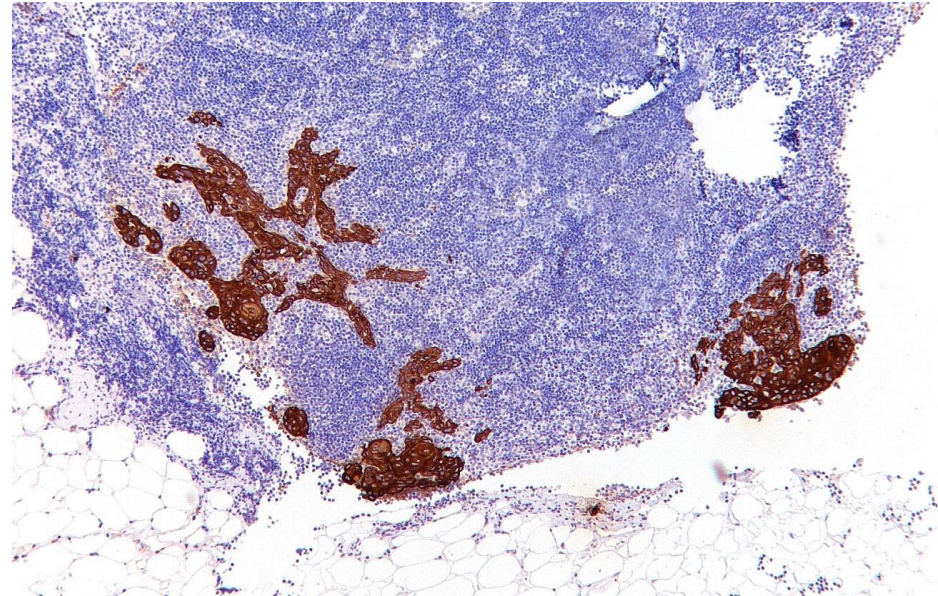
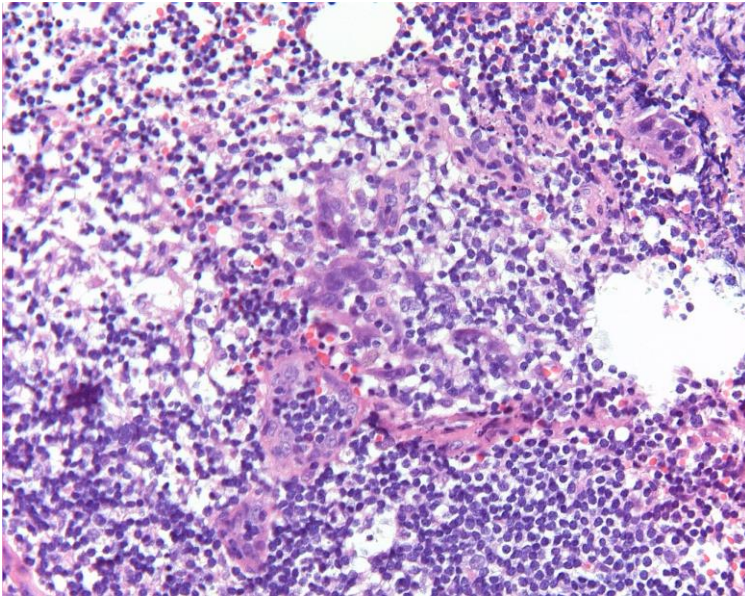




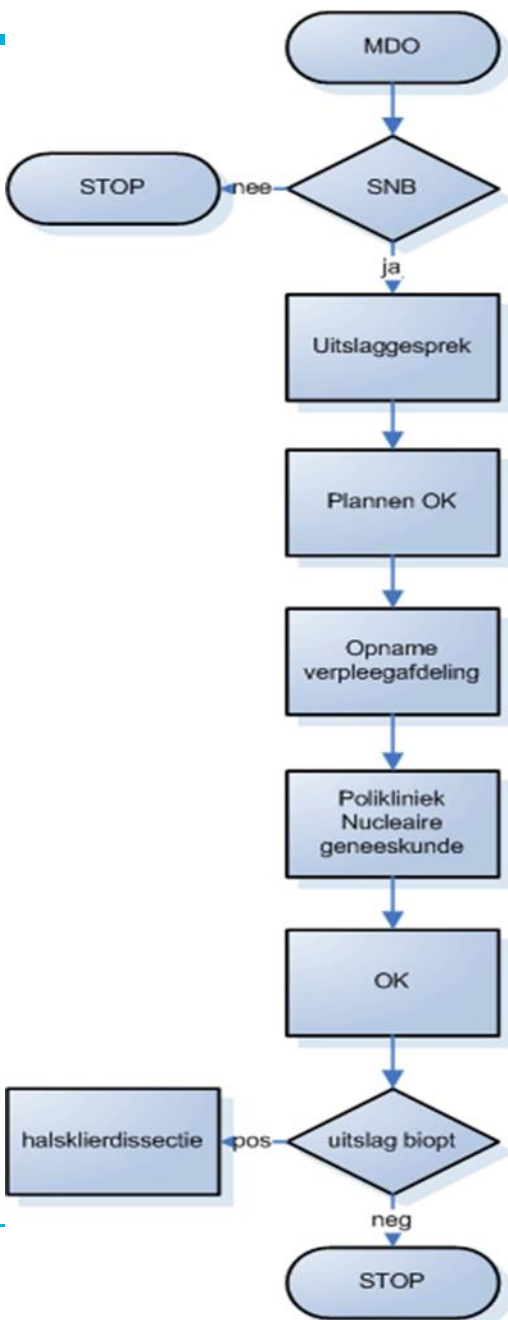
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# Histology

- Metastasis, micrometastasis, isolated tumor cells (ITC)



## Sentinel node biopsy

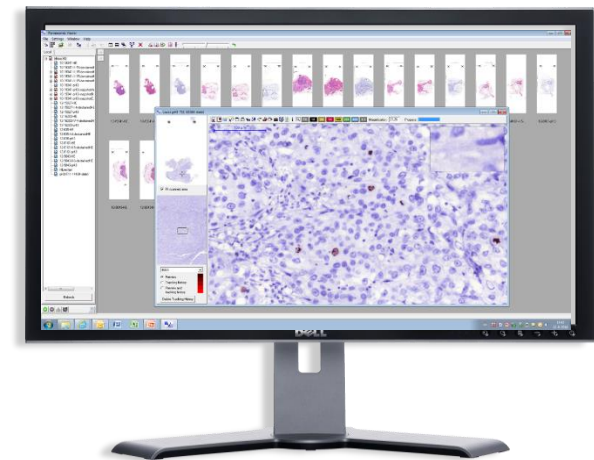


- Sentinel node positive
  - < 4 weeks neck dissection
- Sentinel node negative
  - follow up.

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# Improvement

- Improvement in sentinel lymph node imaging & detection
  - Pre-operative
  - Intra-operative
- Now: 2-stage procedure in case of positive sentinel node
  - Intraoperative assessment (Digital pathology, AI/machine learning)



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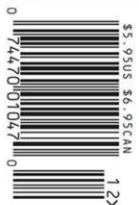
# SUCCESS

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WOODEN**

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