

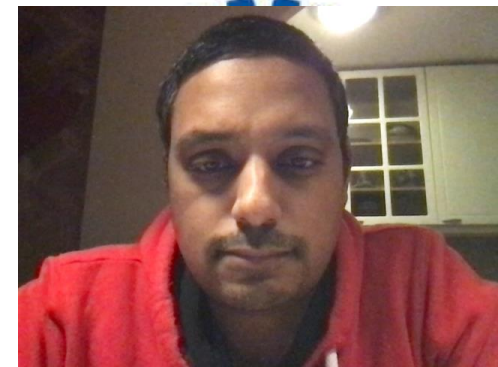
Can patients avoid surgery?

Sheraz R. Markar

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Associate Professor & Deputy Director, SITU, NDS, University
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What do I
say?



Can patients avoid surgery?



WHY?



WHO?



HOW?



WHY?

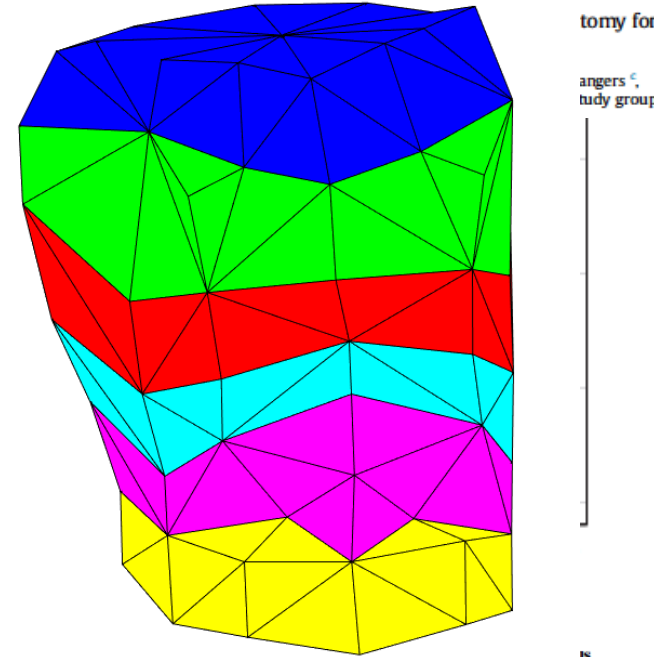
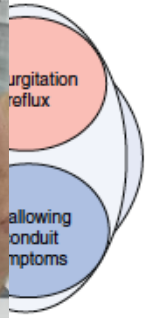


Survivorship - LASER

Patient-reported outcomes after oesophagectomy in the multi-centre international phase III randomised controlled trial of oesophagectomy with or without preoperative chemotherapy and oesophagectomy for oesophageal cancer: a multi-centre international phase III randomised controlled trial

S. R. Markar^{1,2,3}, S. S. Gisbert⁴, N. Ravi⁵, G. I. S. Castro¹⁰, E. Cheong¹⁵, G. B. Hanna¹⁶

J. A. Elliott⁵, C. F. Murphy⁷, C. Greene⁵, M. Pera¹⁰, J. Roigg¹⁰, J. Henegouwen⁶ and

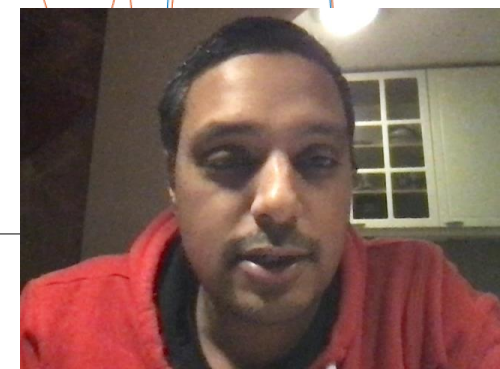
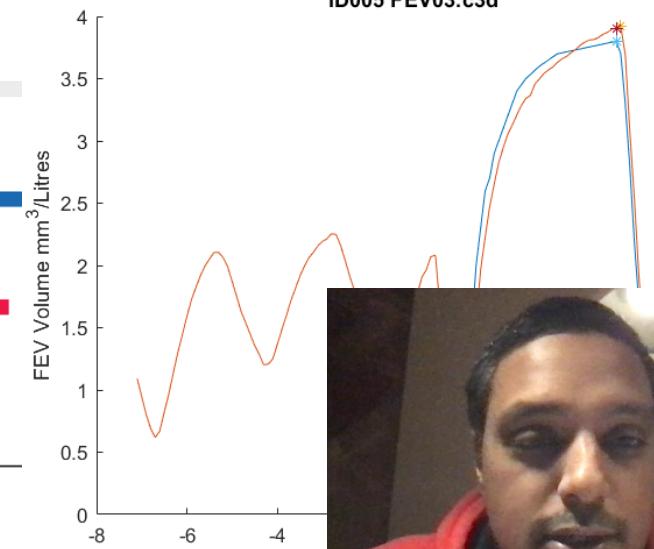


peroperative chemotherapy and oesophagectomy for oesophageal cancer: a

Dun



Early feelin
Reduced



WHO?



- Early-stage cancer

- Complete response



Detection of residual disease after neoadjuvant chemoradiotherapy for oesophageal cancer (preSANO): a prospective multicentre, diagnostic cohort study

Bo Jan Noordman, Manon CW Spaander, Roelf Valkema, Bas PL Wijnhoven, Mark I van Berge Henegouwen, Joël Shapiro, Katharina Biermann, Ate van der Gaast, Richard van Hillegersberg, Maarten C CM Hulshof, Kausilia K Krishnadath, Sjoerd M Lagarde, Grard A P Nieuwenhuijzen, Liekele E Oostenbrug, Peter D Siersema, Erik J Schoon, Meindert N Sosef, Ewout W Steyerberg, J Jan B van Lanschot, for the SANO study group*

Efficacy and safety populations:

61 included in regular biopsy analysis

115 included in bite-on-bite biopsy analysis

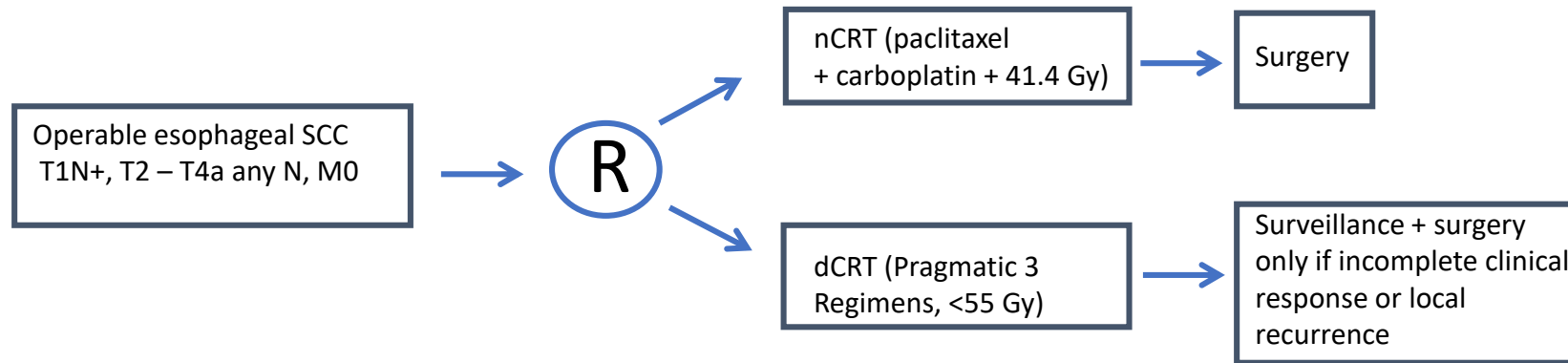
113 included in endoscopic ultrasonography analysis

129 included in PET-CT analysis

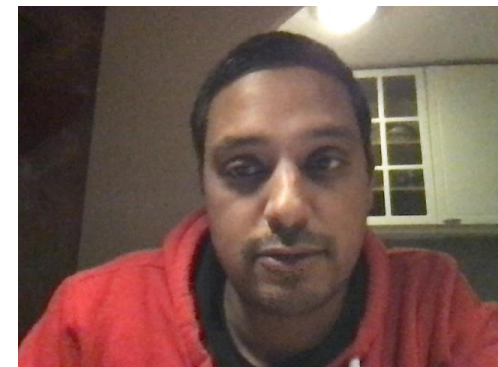
	False-negative cases (95% CI)*	Sensitivity (95% CI)	Specificity (95% CI)	Negative predictive value (95% CI)	Positive predictive value (95% CI)
Endoscopy with regular biopsies and fine-needle aspiration	31% (13–49)	54% (38–70)	69% (44–94)	35% (16–53)	83% (68–98)
Endoscopy with bite-on-bite biopsies and fine-needle aspiration	11% (1–21)	74% (64–83)	77% (59–95)	45% (29–62)	92% (85–99)
Endoscopic ultrasonography with maximum tumour thickness (second clinical response evaluation)	29% (15–43)	59% (48–70)	58% (40–75)	38% (25–52)	76% (64–87)
PET-CT (second clinical response evaluation)	14% (3–24)	82% (73–90)	38% (21–55)	44% (26–63)	



The NEEDS trial



Pragmatic RCT comparing two guideline recommended curative therapy options for oesophageal squamous cell carcinoma



NEO-AEGIS

(NEOADJUVANT TRIAL IN ADENOCARCINOMA OF THE ESOPHAGUS AND ESOPHAGO-GASTRIC JUNCTION INTERNATIONAL STUDY):
 PRELIMINARY RESULTS OF PHASE III RCT OF CROSS VS PERI-OPERATIVE CHEMOTHERAPY (MODIFIED MAGIC OR FLOT PROTOCOL) (CTRIAL-IE 10-14) (NCT01726452)

John V. Reynolds
 Academic Head of Surgery, Trinity College Dublin, Ireland
 Cancer Trials Ireland and Trinity St. James's Cancer Institute



ASCO 2021

ADENOCARCINOMA
 Esophageal and AEG I-III
 cT2-3N0-3M0

EC(O)F(X) x 3 or FLOT x 4 Surgery EC(O)F(X) x 3 Or FLOT x 4 Arm A

Neo CRT (CROSS) wCP-RT(41.4Gy)+Surgery Arm B

Non-inferiority

[(n= 540) -powered as per first futility analysis (n=71 deaths) in December 2018]

Primary endpoint:
 Overall survival

Secondary end points:
 Disease free survival
 Time to treatment failure
 TRG
 R0
 Toxicity
 Postoperative complications

Stopped for futility at 362

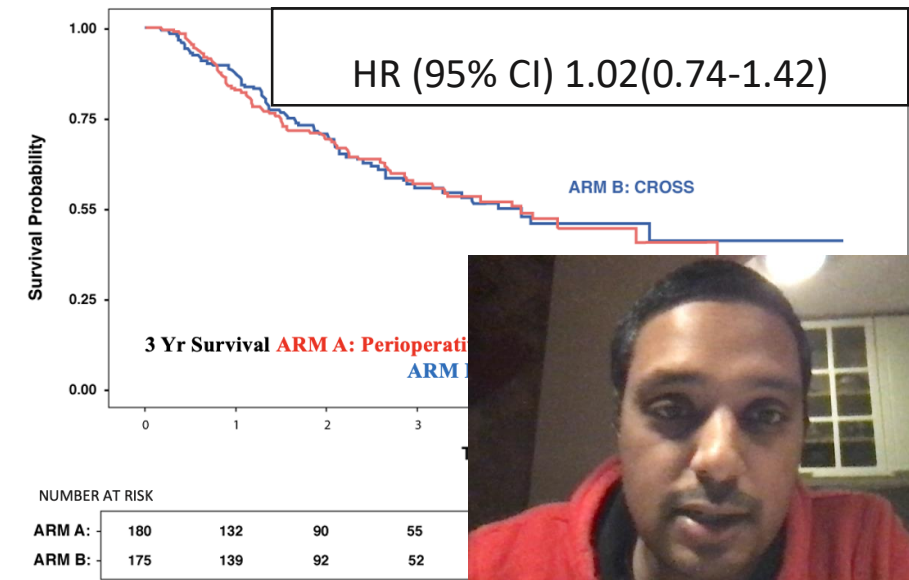
Results: Demographics and Surgical Approach

	ARM A (Chemo) N = 184	ARM B (CROSS) N = 178
Median (range) age	64 (35-83)	64 (45-81)
Male	91.8%	88.8%
MAGIC/FLOT	157/27	-
cT3	84%	84%
cN 1-3	60.3%	56%
Surgical Approach		
Transthoracic Esophagectomy	75%	80%
Transhiatal	1.2%	4.3%
Extended gastrectomy	5.8%	5.1%
MIE	18%	11.7%

Pathological Outcomes
 ALL IN FAVOUR OF nCRT

ypN0 (p=0.004)
 pCR (p=0.001)
 R0 (p< 0.001)
 TRG (p< 0.001)

Overall Survival



Courtesy of John Reynolds, Trinity College Dublin

Summary: Prognosis of pCR after nCT vs. nCRT

- Multi-centre study; 8 international HV centers.
- 465 patients pCR; 132 nCT vs. 333 nCRT

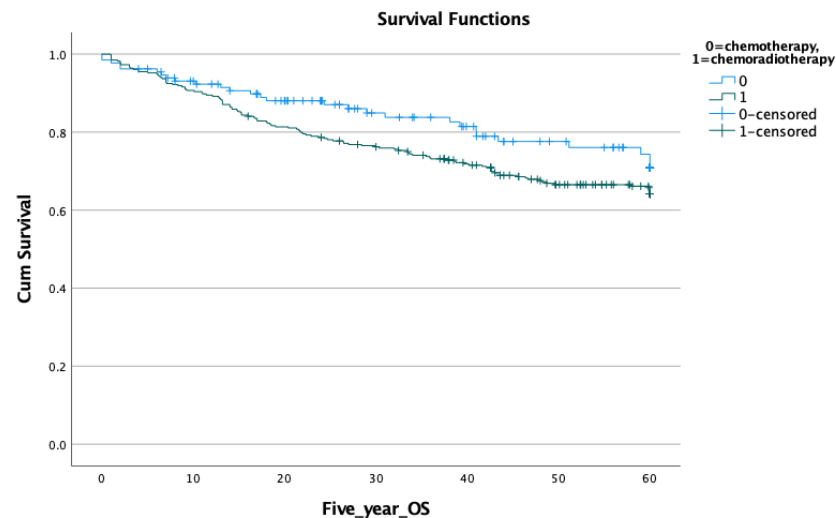
5yr OS

nCT 78.8%

nCRT 65.5%

P value = 0.099

MVA HR 1.19, 95% CI 0.77 to 1.84



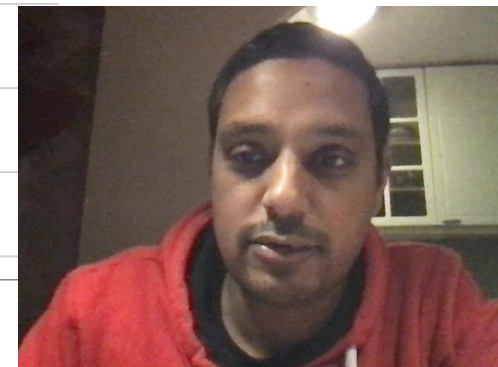
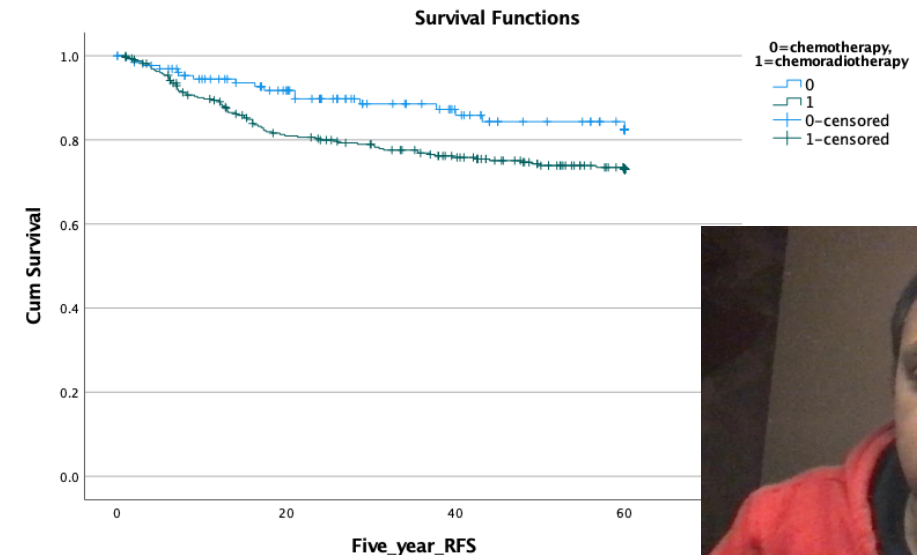
5 yr RFS

nCT 87.1%

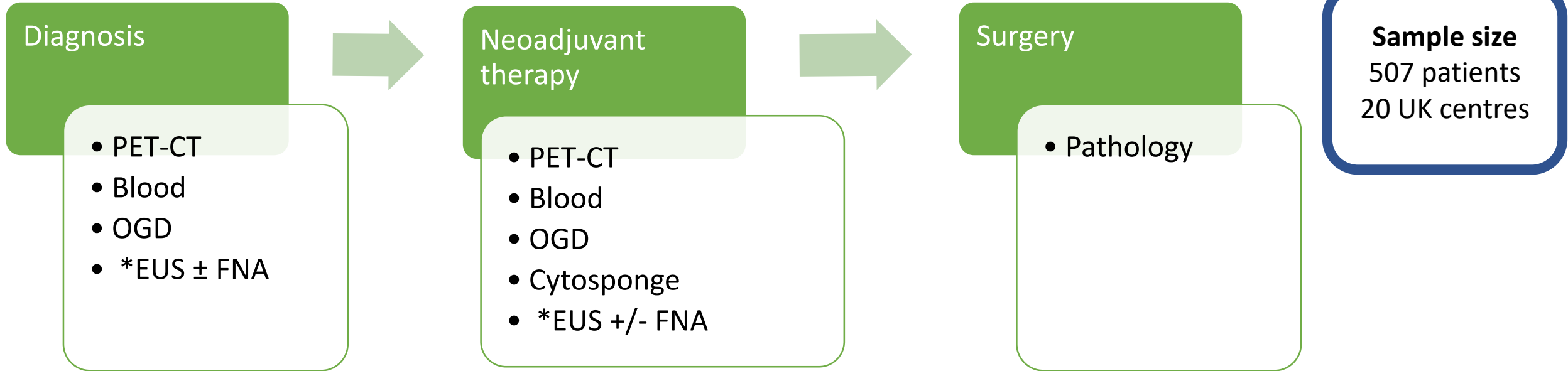
nCRT 75.3%

P value = 0.026

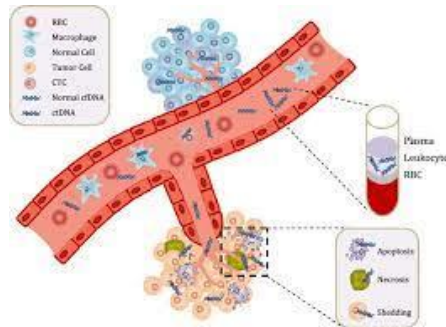
MVA HR 1.70, 95%CI 1.22 to 2.99



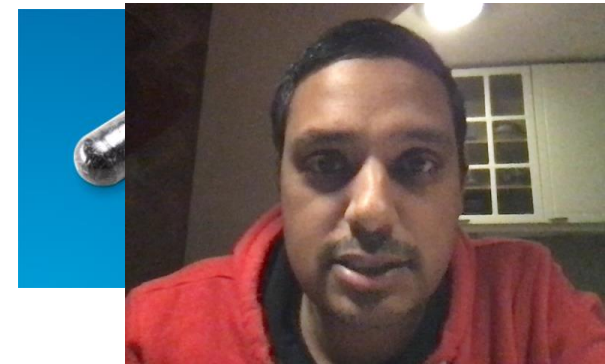
Assessment of Response after Systemic Therapy for Oesophageal cancer (ARESTO)



Systemic



Local / Intra-oesophageal





HOW?

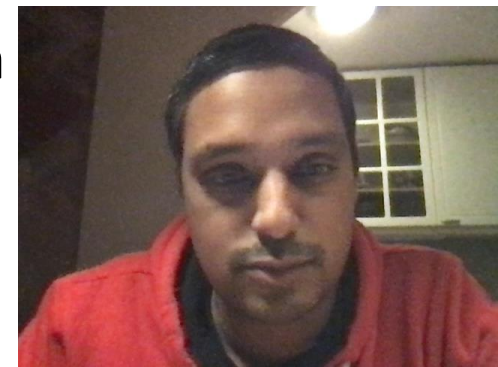


Thoracolaparoscopic dissection of esophageal lymph nodes without esophagectomy is feasible in human cadavers and safe in a porcine survival study

DOTE 2016


H. T. Künzli,^{1,2} M. van Berge Henegouwen,³ S. Gisbertz,³ C. Seldenrijk,⁴ K. Kuijpers,⁴ J. Bergman,²
M. Wiezer,⁵ B. Weusten,^{1,2}

- High risk T1b esophageal adenocarcinoma
 - Submucosal invasion >500nm, poor differentiation, and/or lymphovascular invasion
- Currently treated with esophagectomy
 - Risk of lymph node metastases 0 – 37%
- If radical (R0) endoscopic resection is achieved
 - Feasible and safe to only perform lymphadenectomy
- In 5 human cadavers and 5 swine: only lymphadenectomy
 - Median 26 nodes in cadavers; retained lymph nodes: 1 LN in 2/5, tech
 - Ischaemia/stenosis in swine that survived 28 days: 0%
 - 1 pig died during the procedure of ventricular fibrillation

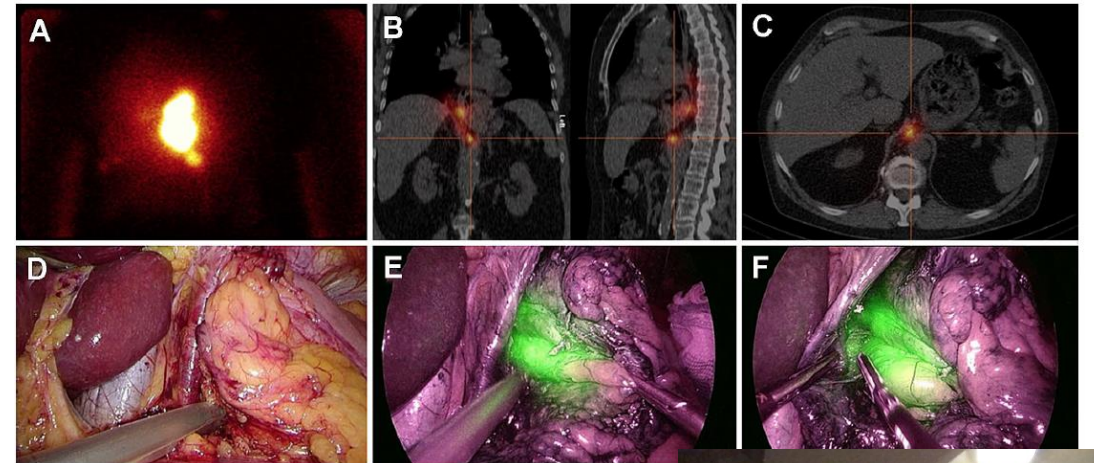


Feasibility of sentinel node navigated surgery in high-risk T1b esophageal adenocarcinoma patients using a hybrid tracer of technetium-99 m and indocyanine green

Surg Endos 2022

Anouk Overwater^{1,2}  · Bas L. A. M. Weusten^{1,2} · Jelle P. Ruurda³ · Richard van Hillegersberg³ · Roel J. Bennink⁴ · Bart de Keizer⁵ · Sybren L. Meijer⁶ · Lodewijk A. A. Brosens⁷ · Roos E. Pouw⁸ · Jacques J. G. H. M. Bergman⁸ · Mark I. van Berge Henegouwen⁹ · Suzanne S. Gisbertz⁹

- 5 patients
- SNNS with ICG + 99mTc followed by esophagectomy
- SNs detected in all patients, median 3
- High concordance between pre- & intraoperative SN detection
 - In 2 patients additional peritumoral SNs identified with ICG
- No (micro)metastases

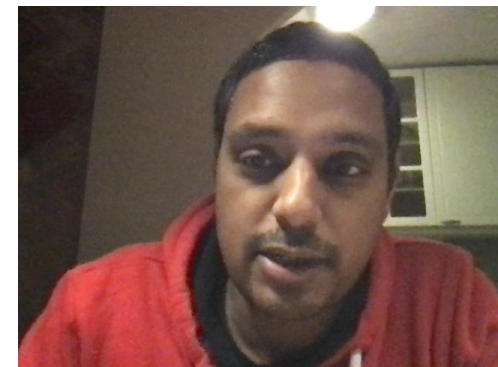


Current studies

SNAP III, IV and more

SNAP III: 10 patients cT1b

- Only SNNS after radical endoscopic resection of high risk T1b EAC
- Endpoints: morbidity, esophago-gastric function, recurrence, detectable SN, number of SNs, QoL, survival
- SNAP IV: 5 patients cT1N1
 - Rate of tumor-positive LN(s) detected as SN(s)
 - Either on SPECT/CT, probe-based or with a NIR camera
- Future plans
 - Large cohort study



Surveillance of Clinically Complete Response

NO Robustly developed protocol

Clear evidence gap to be addressed

Needed before moving towards watch and wait strat



Questions

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