Molecular imaging guidance of surgical procedures

(review and current status)

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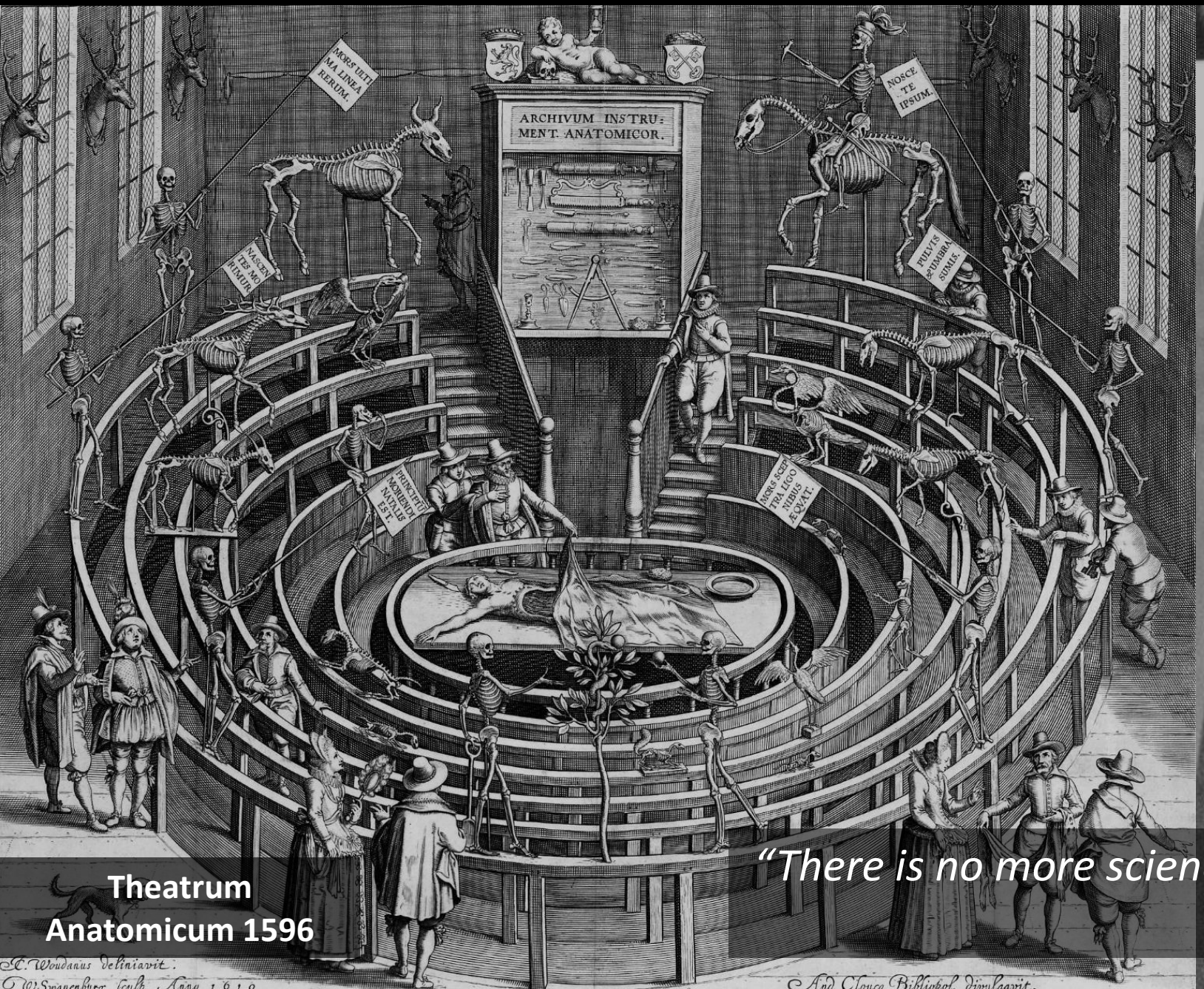
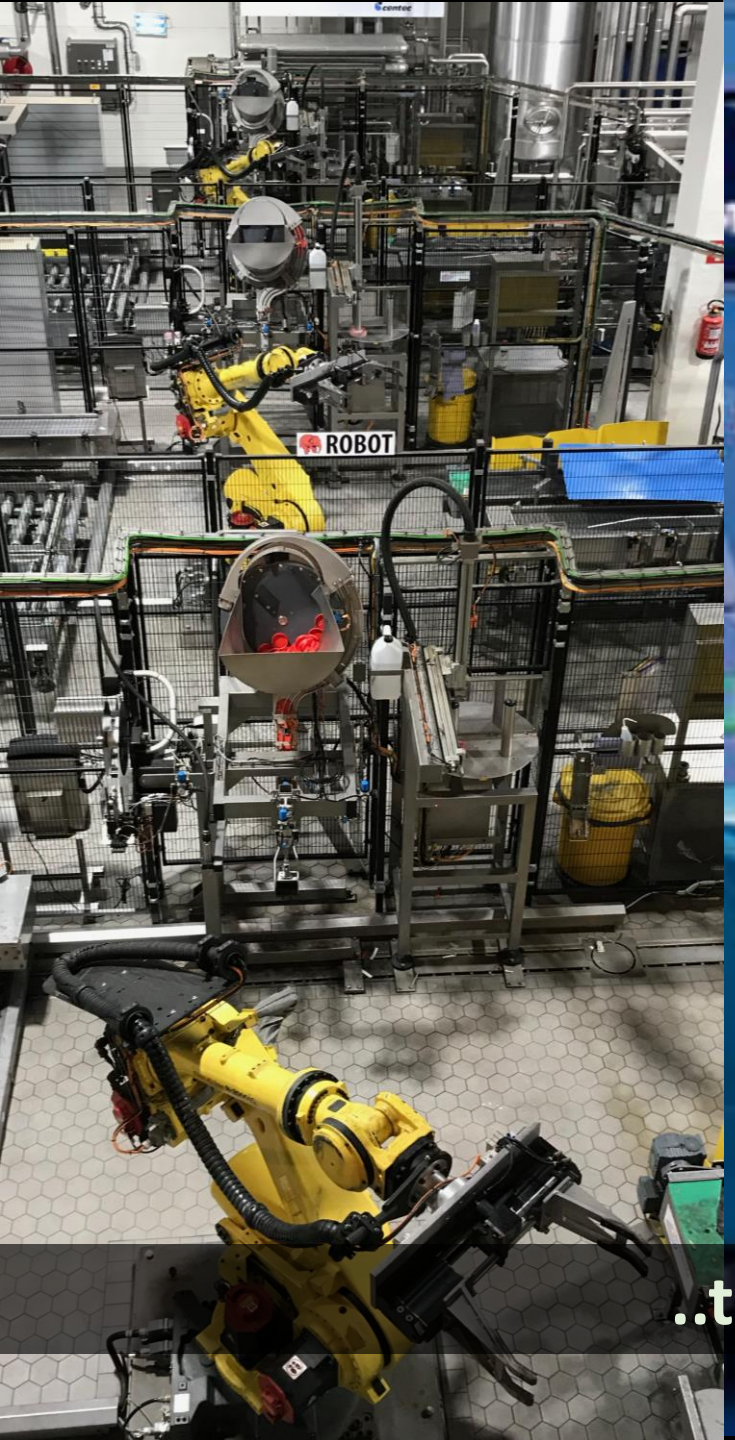
Precision medicine has evolved from invasive surgery in the past ..

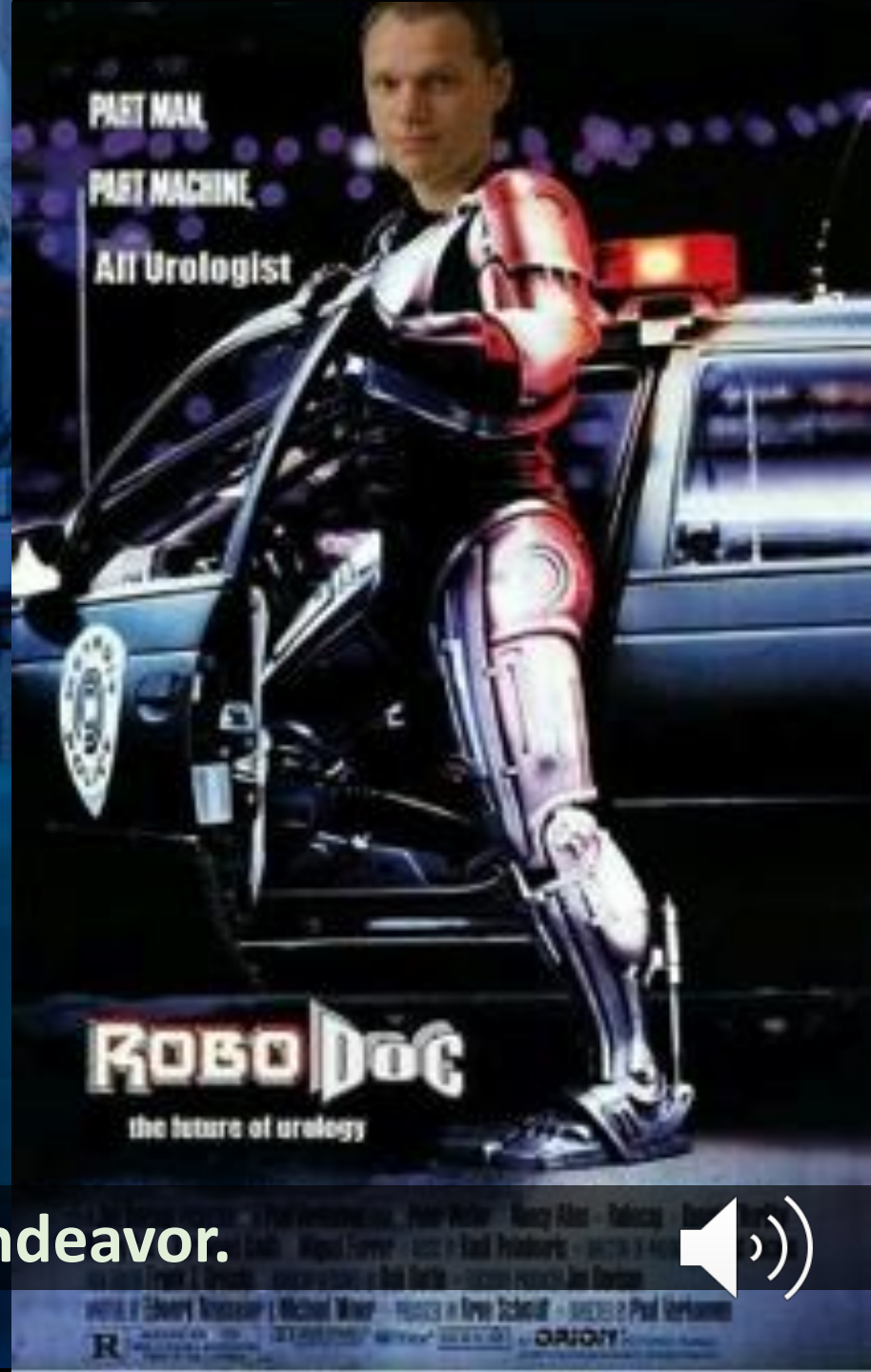


Theatrum Anatomicum 1596

"There is no more science to surgery that to butchering"

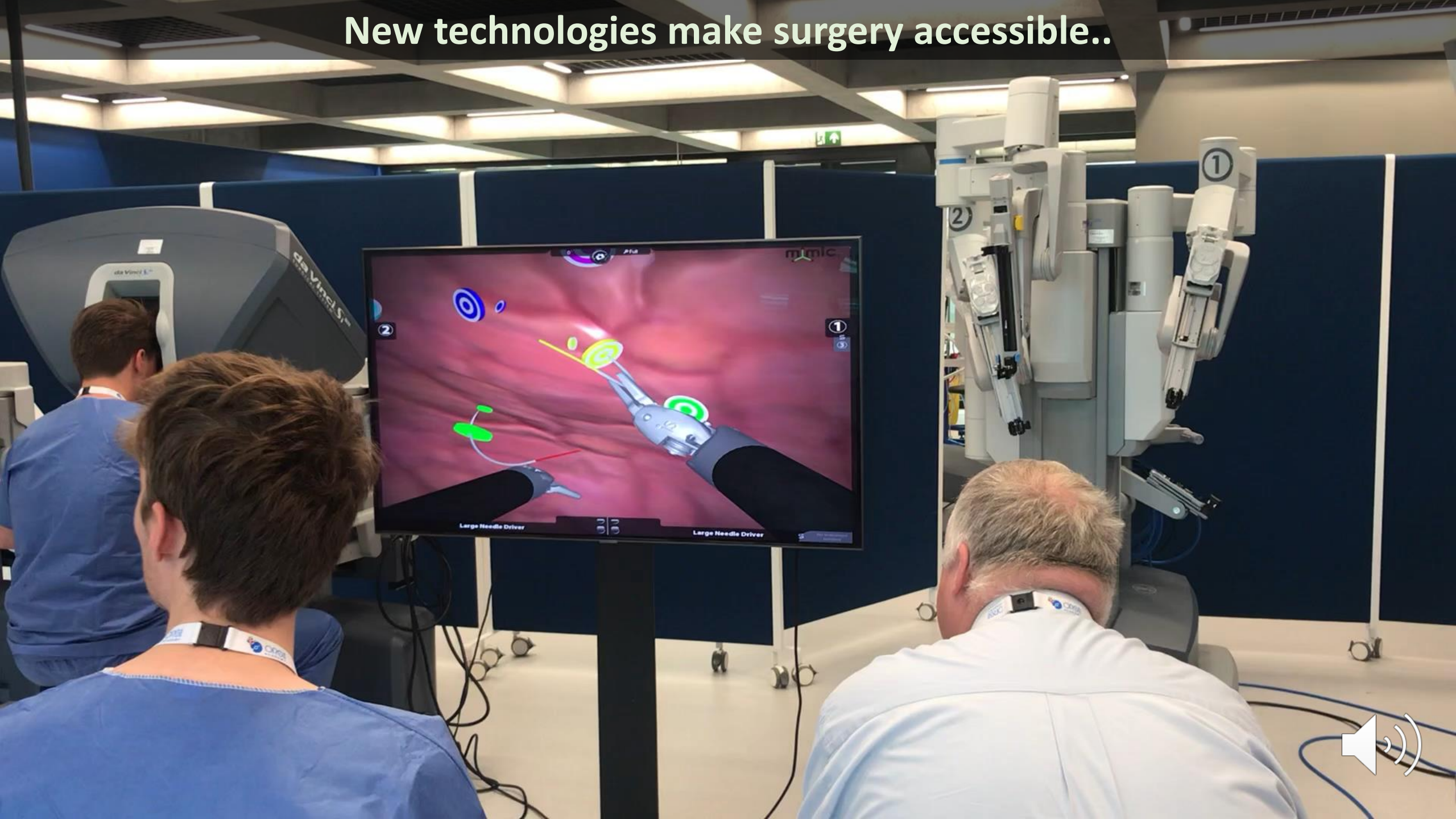
Edward Thurlow 1811



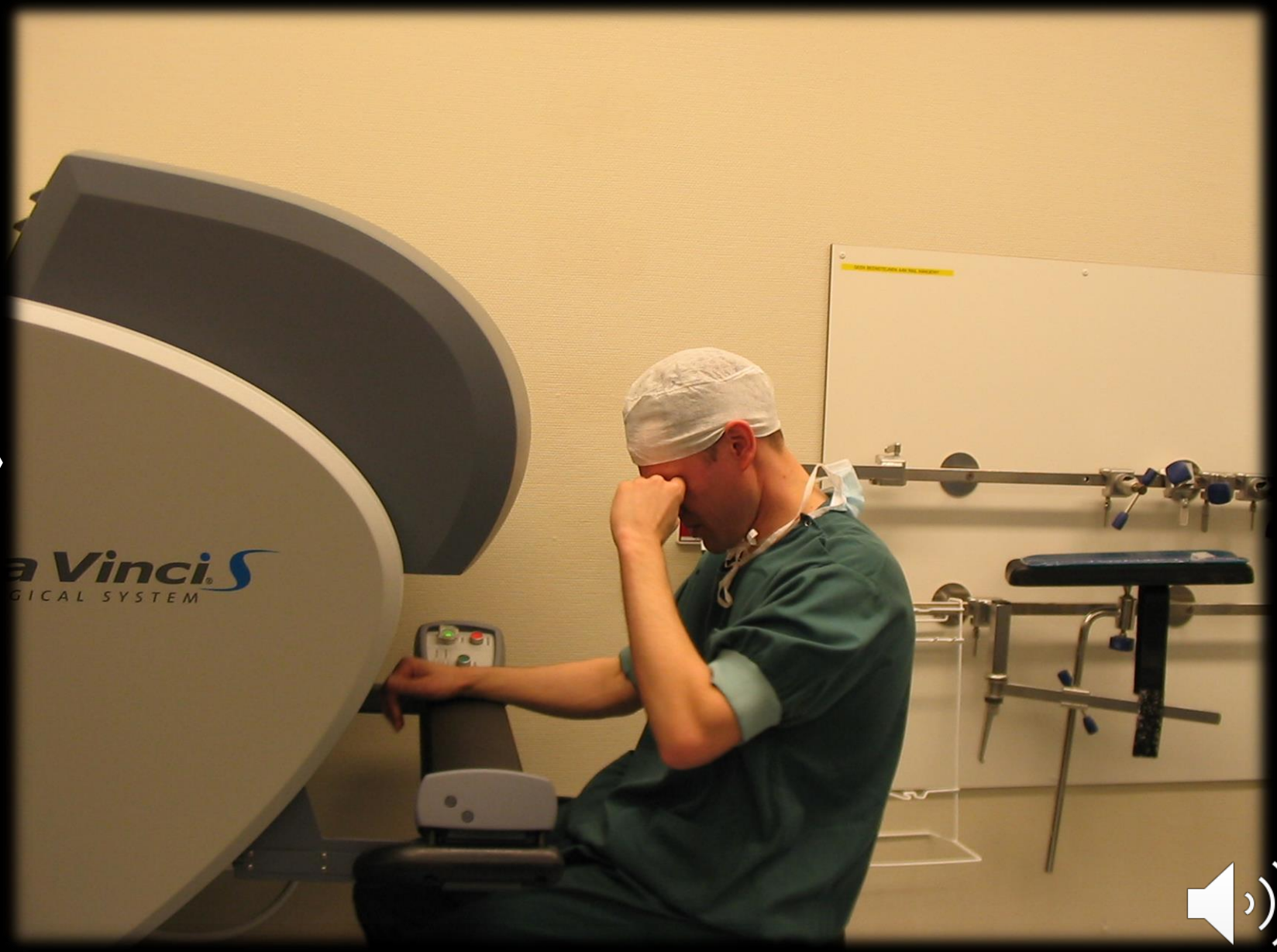


..to a highly refined technical endeavor.

New technologies make surgery accessible..



.. But pinpointing targets for surgeons to resect remains a challenge



van der Poel et al., *Eur Urol* **2011**, Buckle et al., *J Nucl Med* **2012**

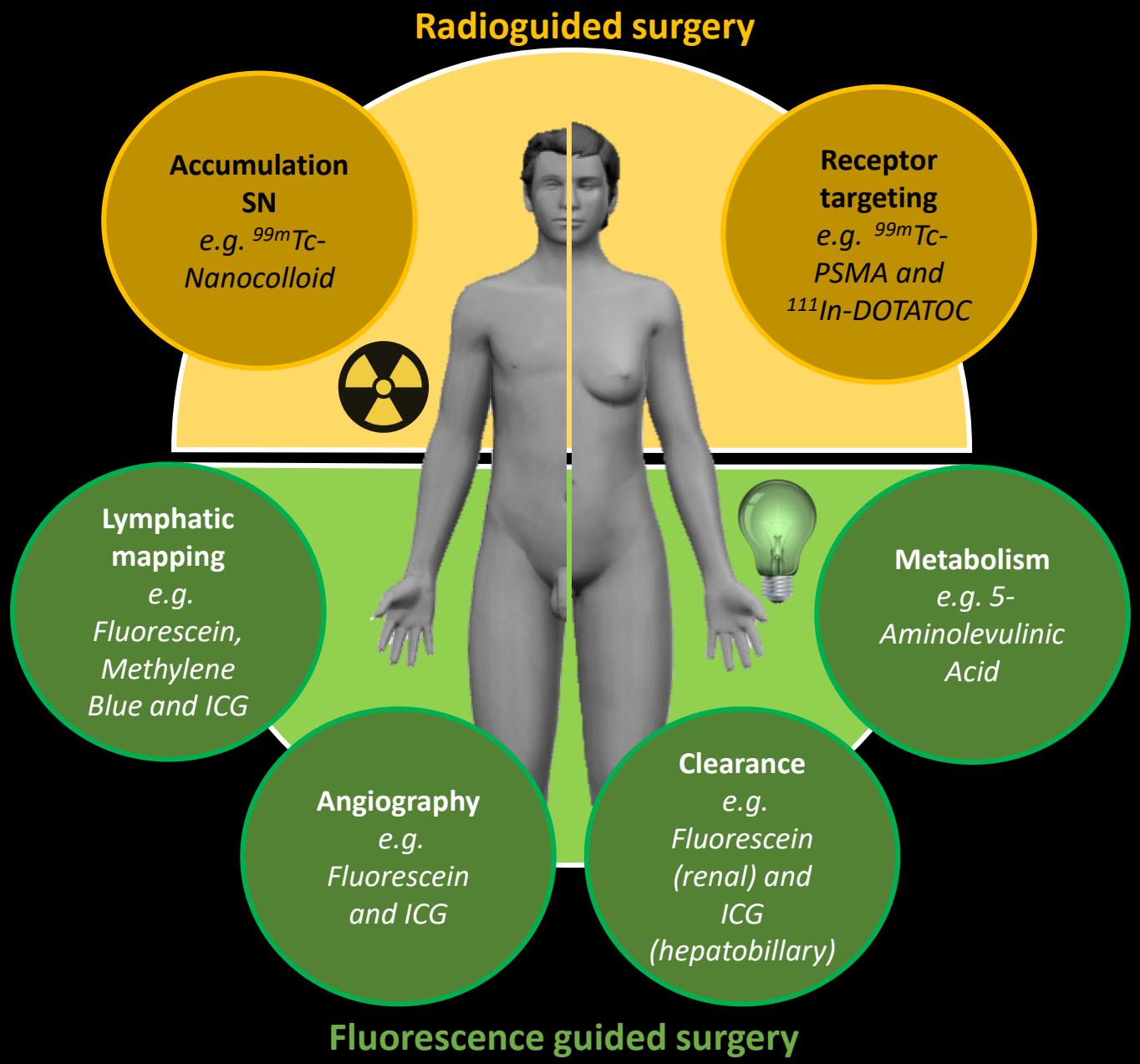
Interventional molecular imaging – a multidisciplinary approach

Imaging technologies can help differentiate between benign and malignant tissue…

…by illumination specific features

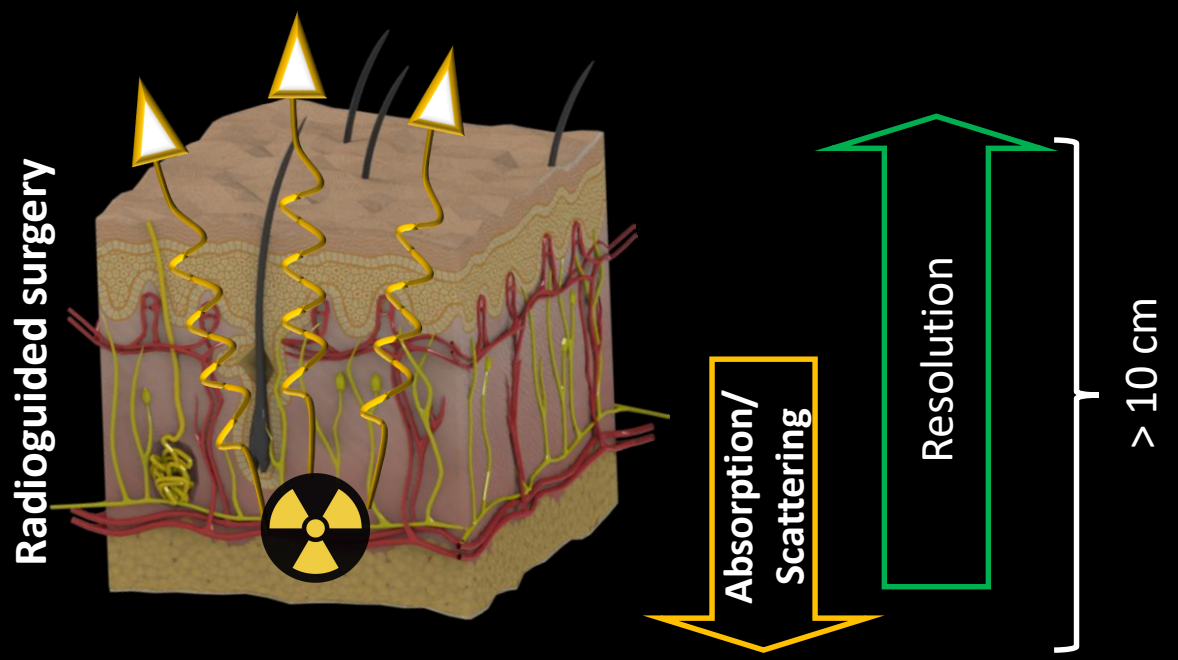
Like any intervention it is essential to pick the right tools for the job

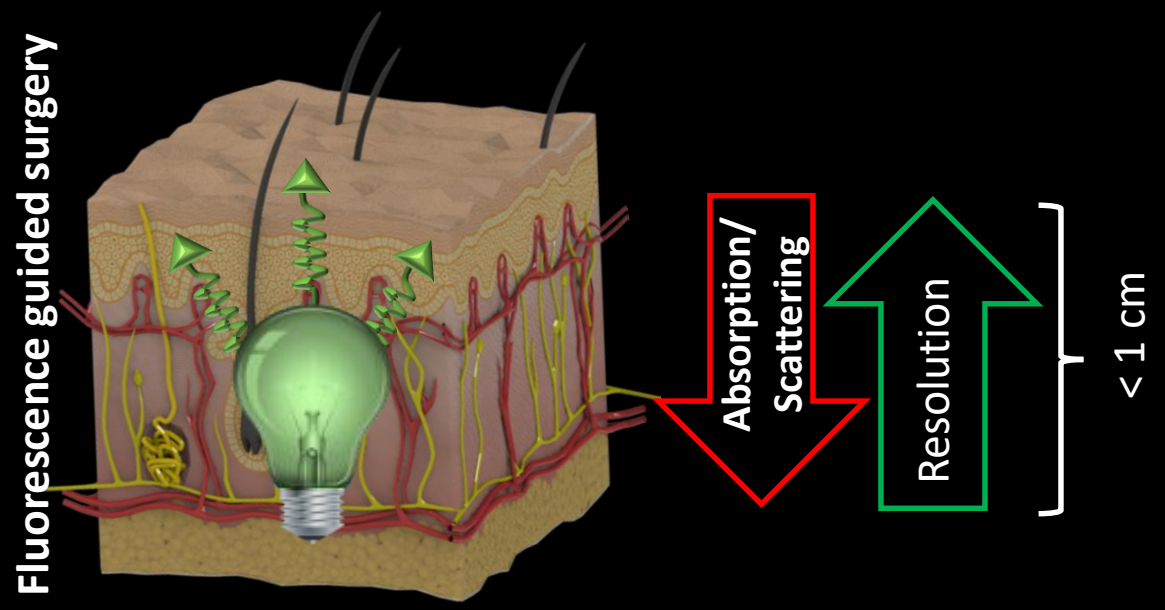
Interventional molecular imaging: Radioguided surgery vs. Fluorescence guided surgery

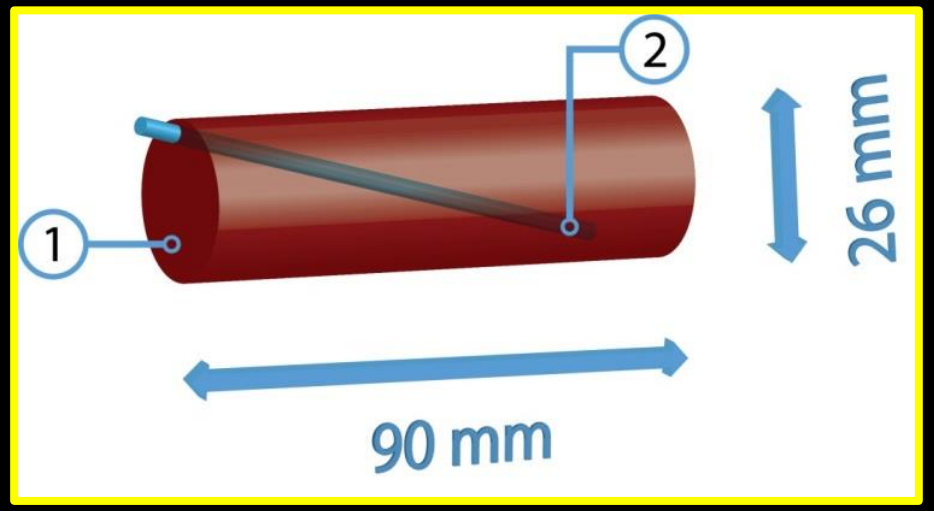


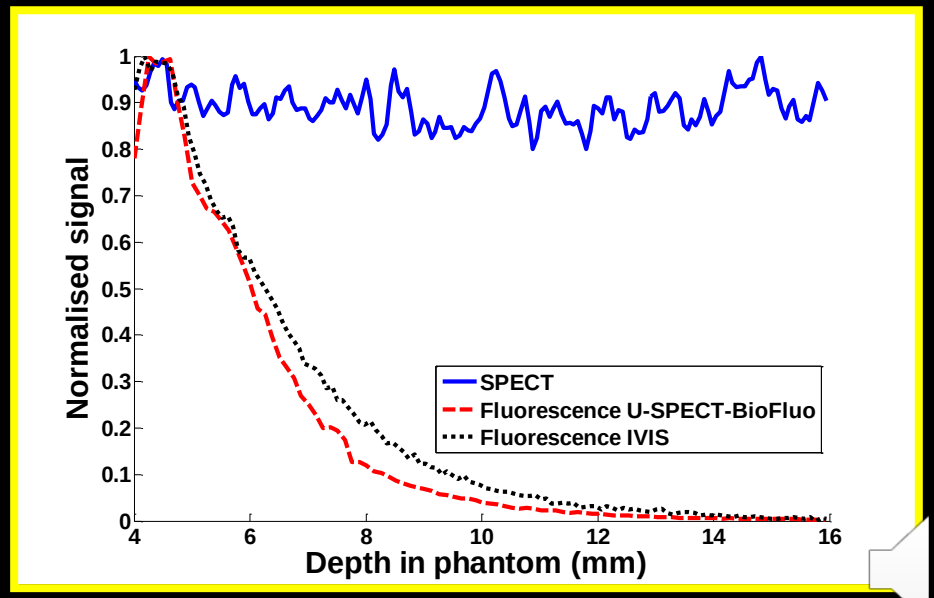
Van Leeuwen et al. JNM 2020

Penetration depth: Radioactive vs. Fluorescence signals



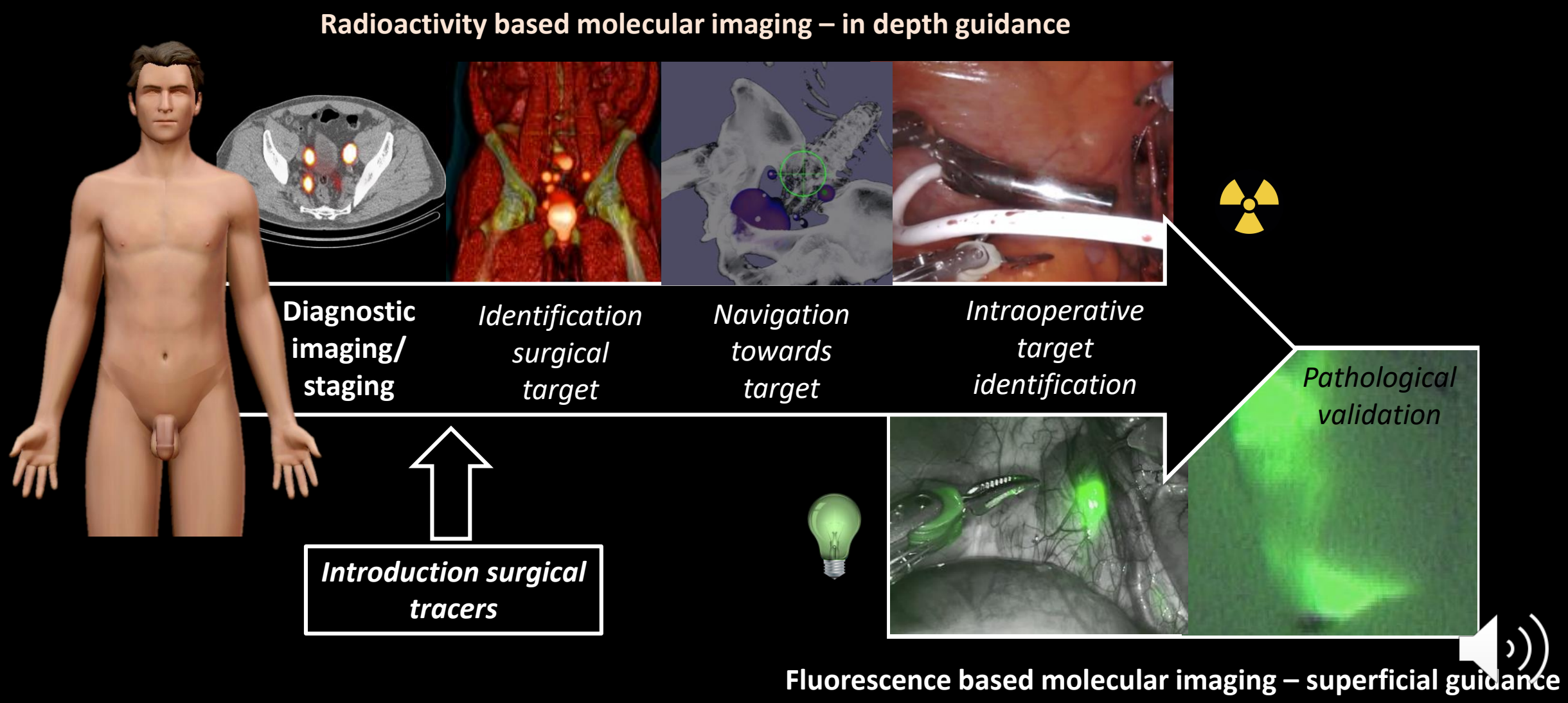




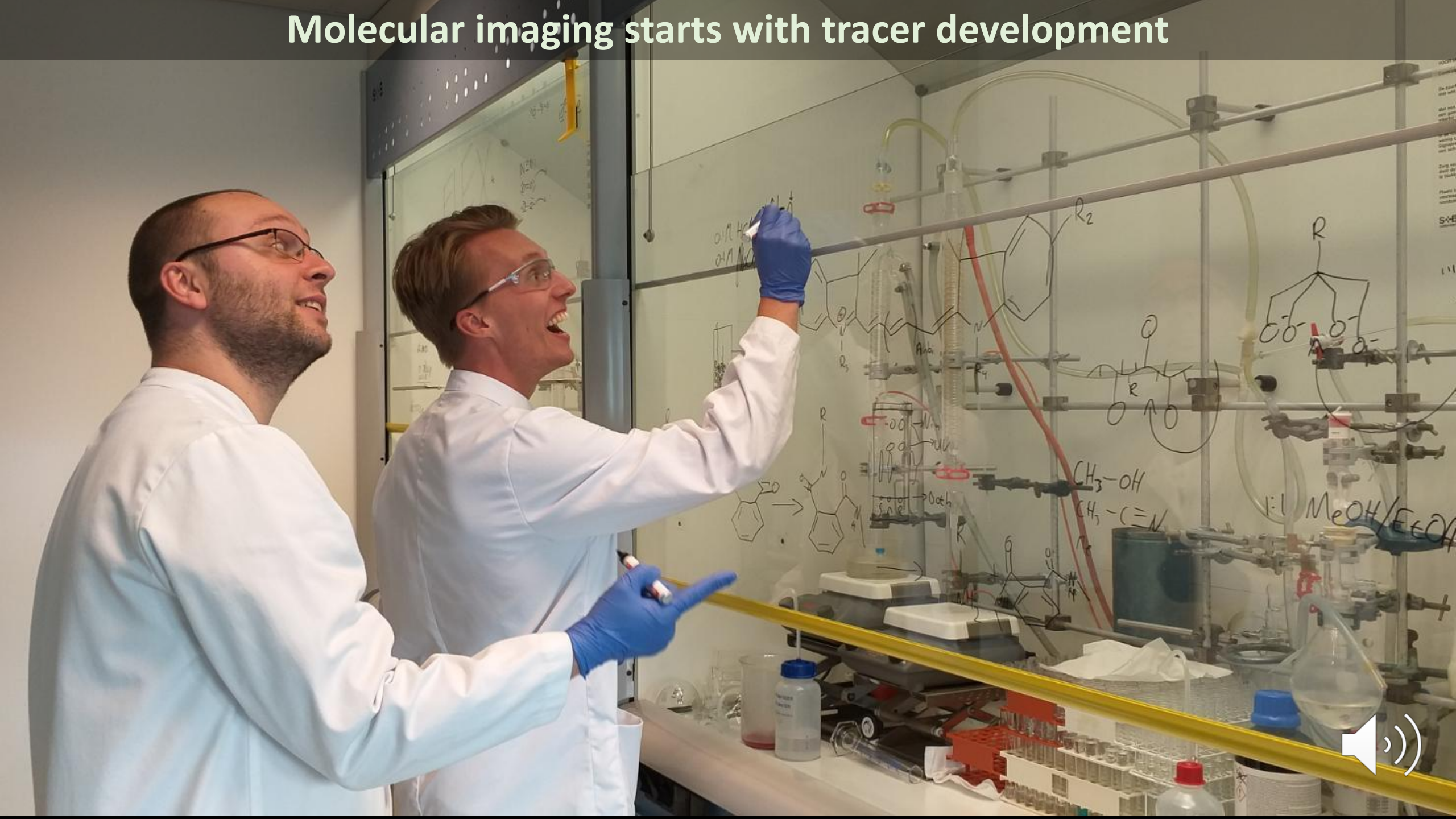


Van Oosterom et al., EJNMMI Research **2014**

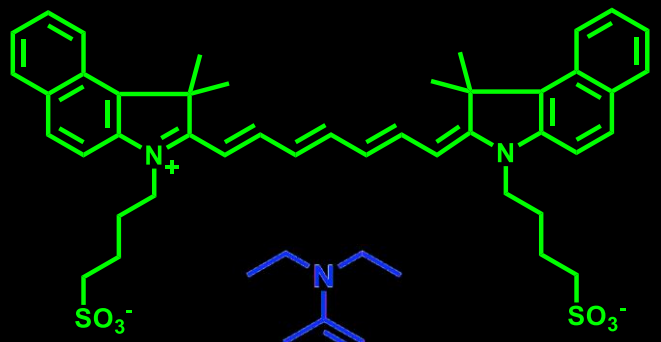
Hybrid approaches that combine radio- and fluorescence guidance help address the full surgical complexity

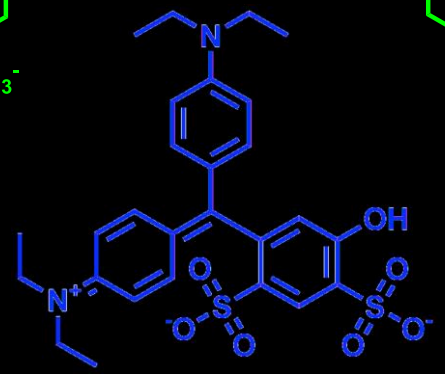


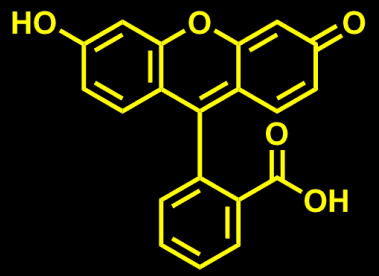
Molecular imaging starts with tracer development



Lymphatic imaging: chemical properties dictate physiology and molecular uptake

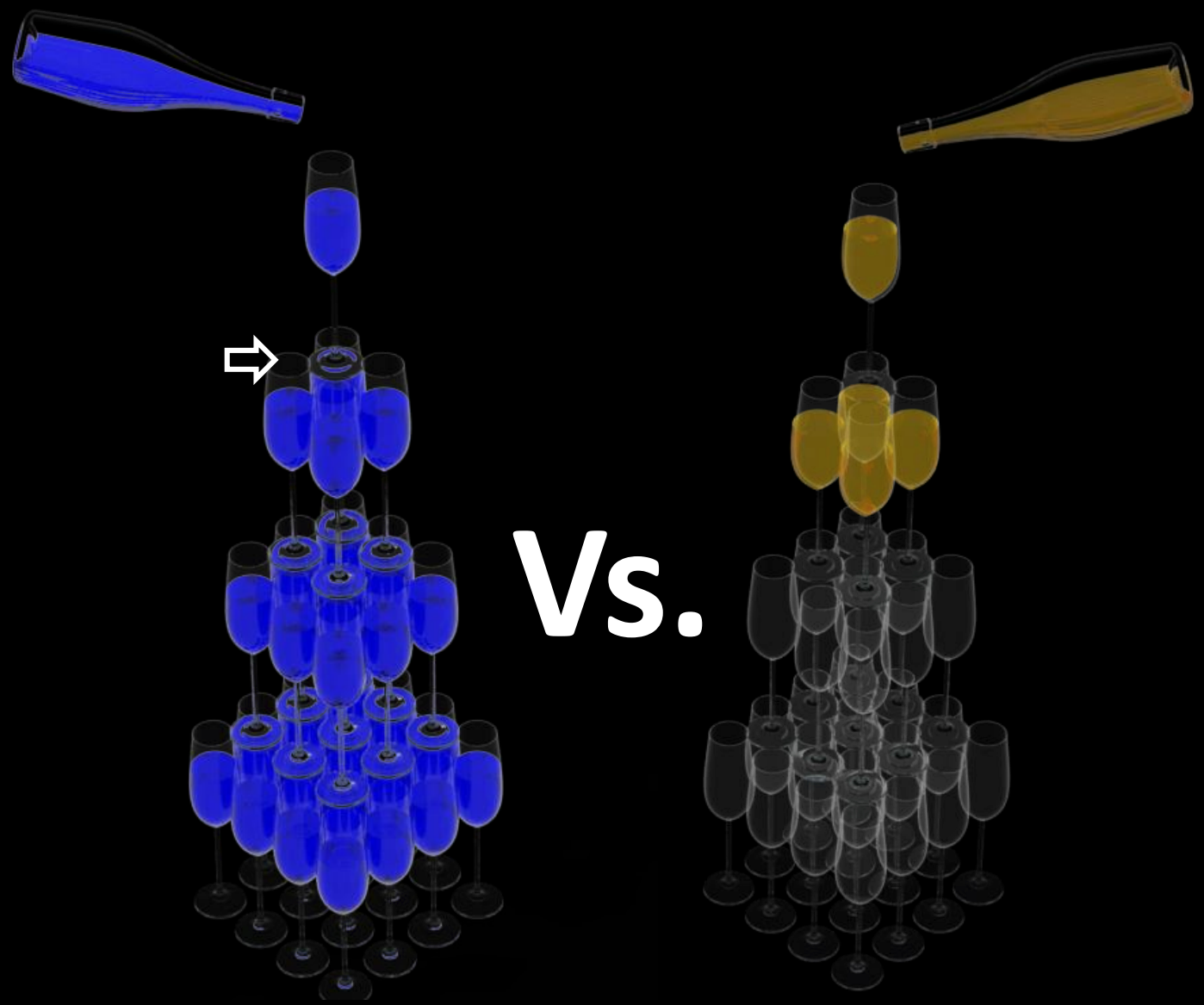






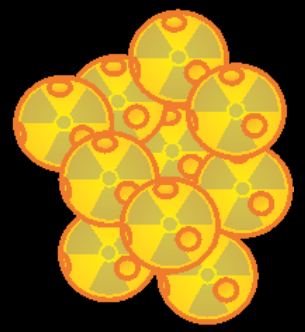
(-) Rapid clearance
(no specificity)

(+) Optical
identification



Vs.

vd Berg et al QJNMMI **2014**

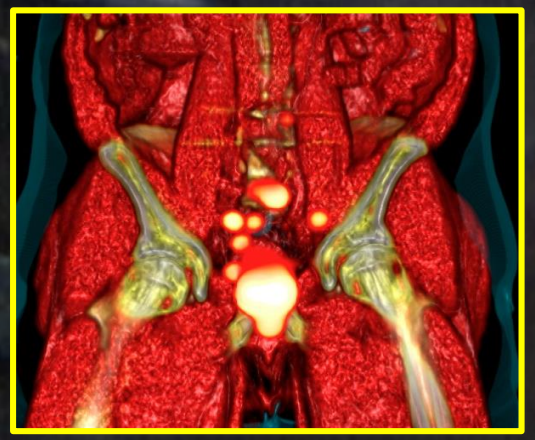


(+) SN specificity

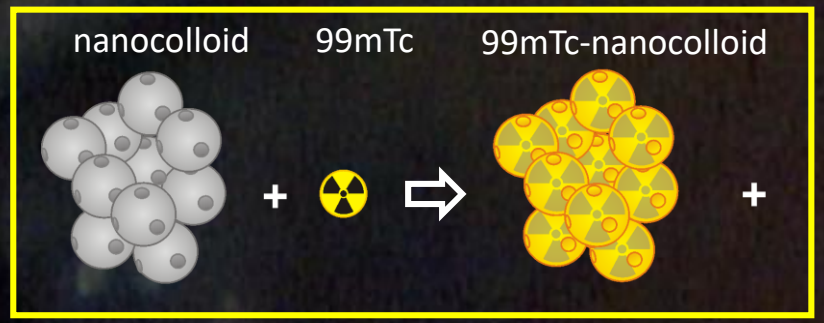
(+) Long retention
(> 30h after tracer
administration)

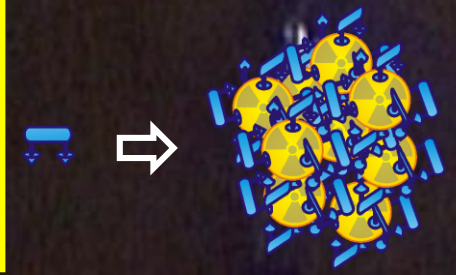
(+) Preoperative
imaging

Hybrid tracers help combine the best of both worlds e.g. ICG-^{99m}Tc-nanocolloid



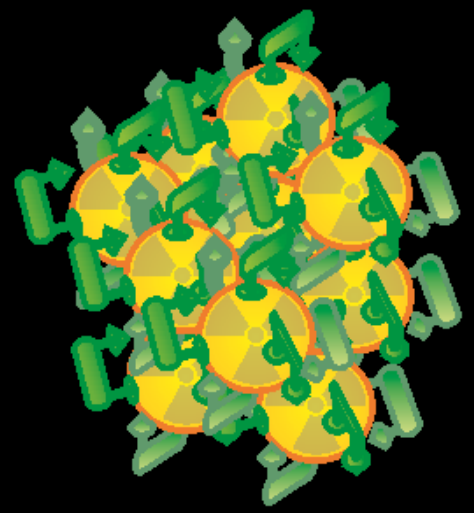
"standard" in Europe





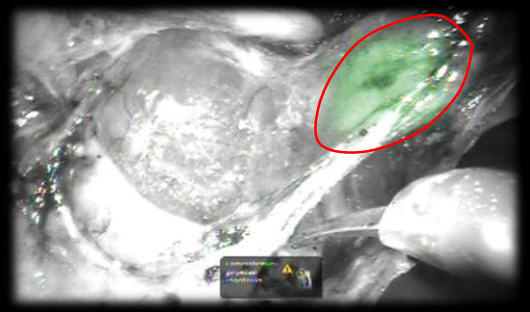
van der Poel et al., *Eur Urol* **2011**

The complementarity of the imaging signatures can be used to realize precision surgery

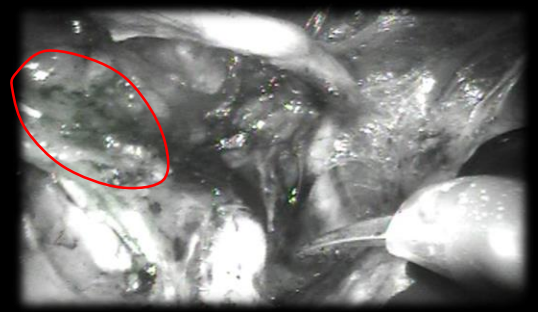


ICG-^{99m}Tc-nanocolloid
(radioactive and fluorescent)

Fluorescence imaging only

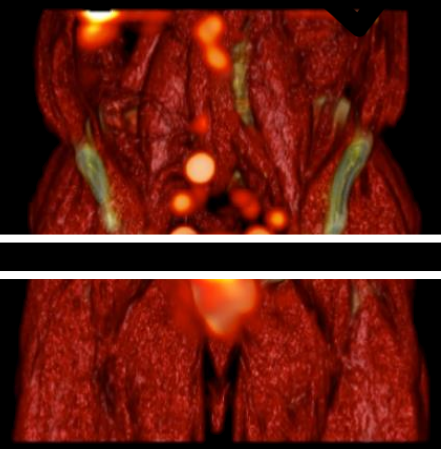


48%

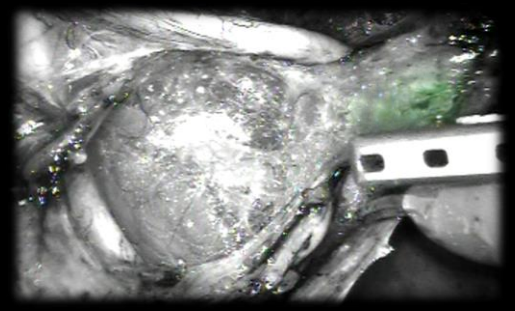


52%

Unblinding SPECT/CT



Fluorescence imaging

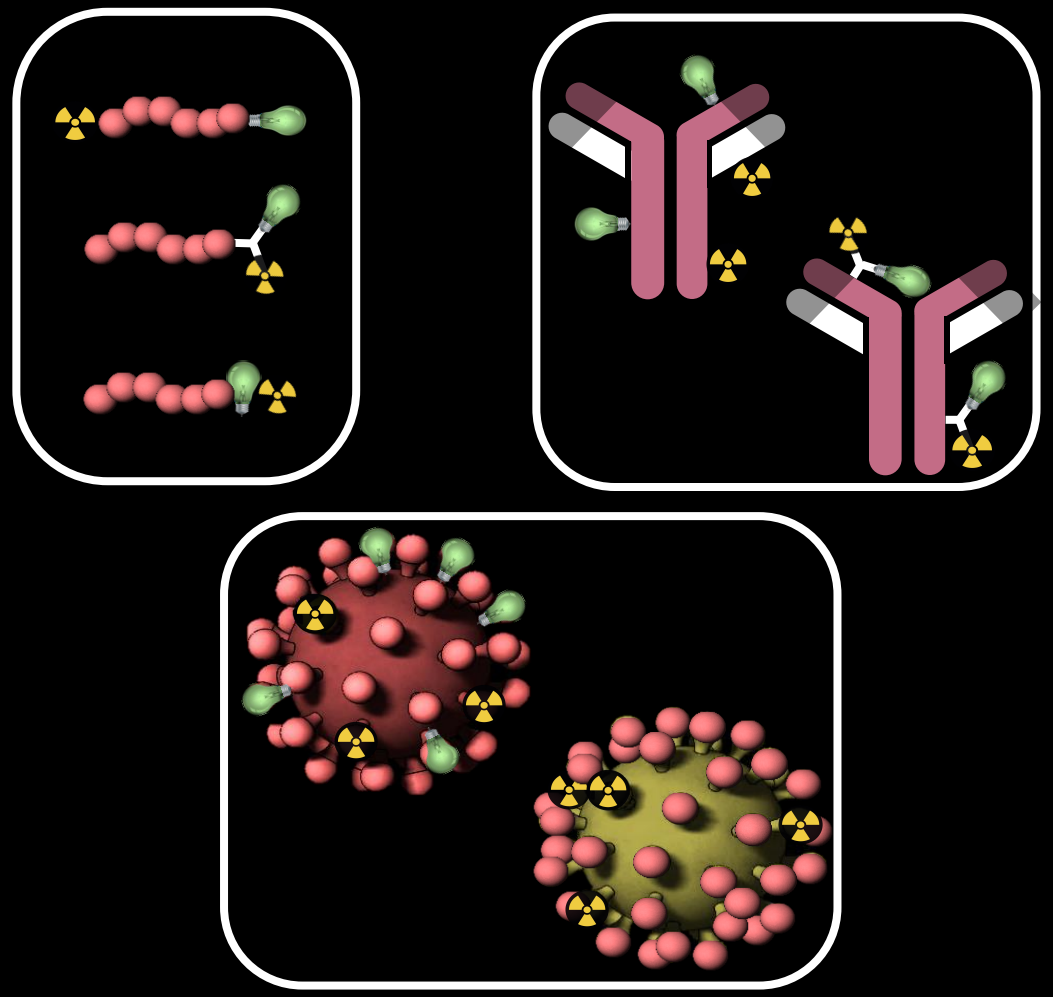


100%

Meershoek et al. JNM 2019

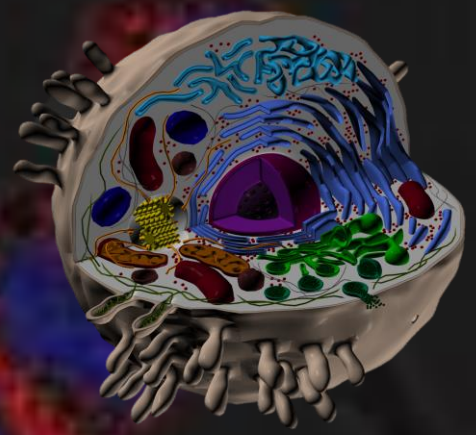
The concept of using hybrid tracers in clinical trails is gaining traction

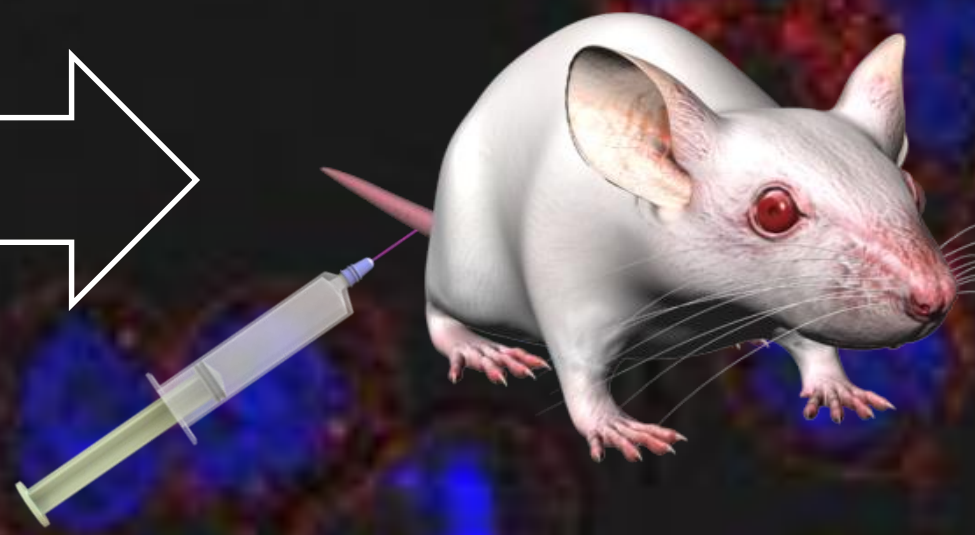
Hybrid tracer	Number of patients
ICG-^{99m}Tc-nanocolloid	>1500
^{131}I-Fluorescein	>20
$^{123/125}$I-methylenen blue	>20
111In-DOTA-gerentuximab-IRDye800CW	>15
^{68}Ga-IRDye800CW-BNN	>14
FITC-^{125}I-CEA mAb	> 5
^{124}I-cRGDY-PEG-C	>5
Cerenkov	>60

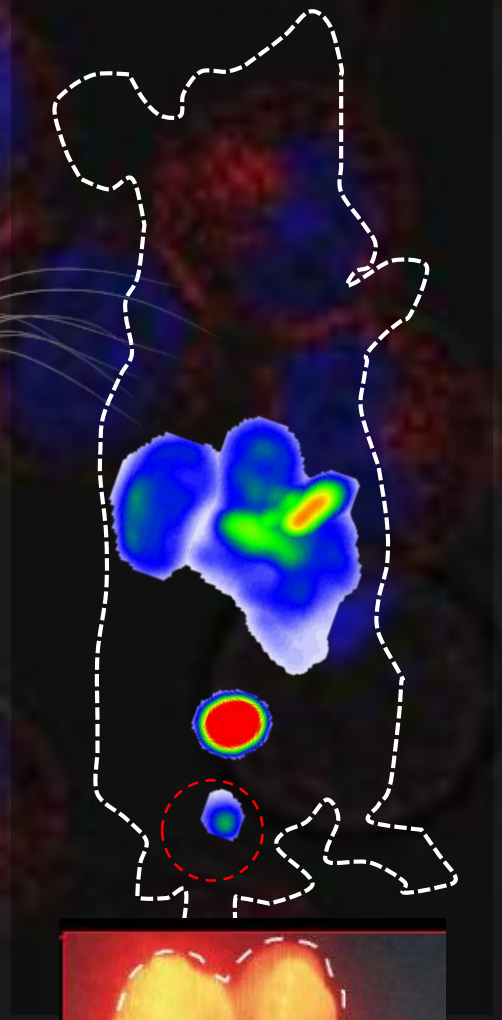


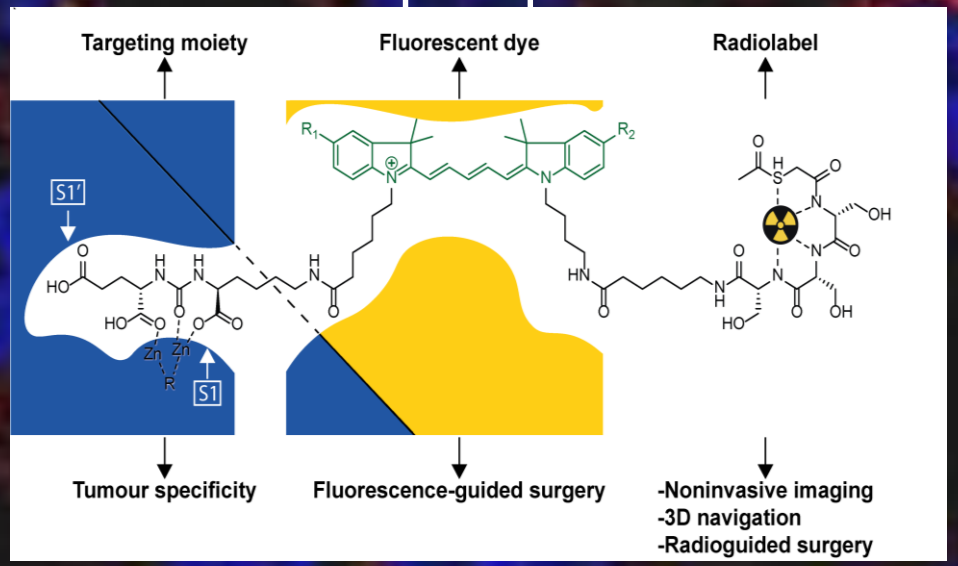
Van Leeuwen et al. JNM 2020

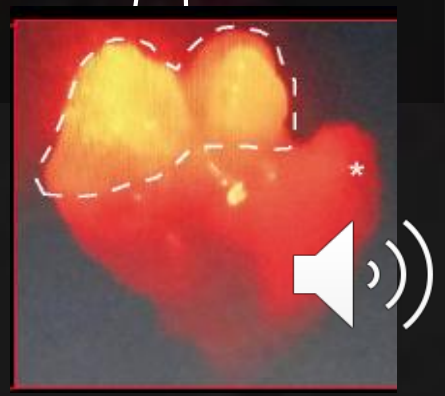
Various preclinical developments are ongoing e.g. Cy5-^{99m}Tc-PSMA







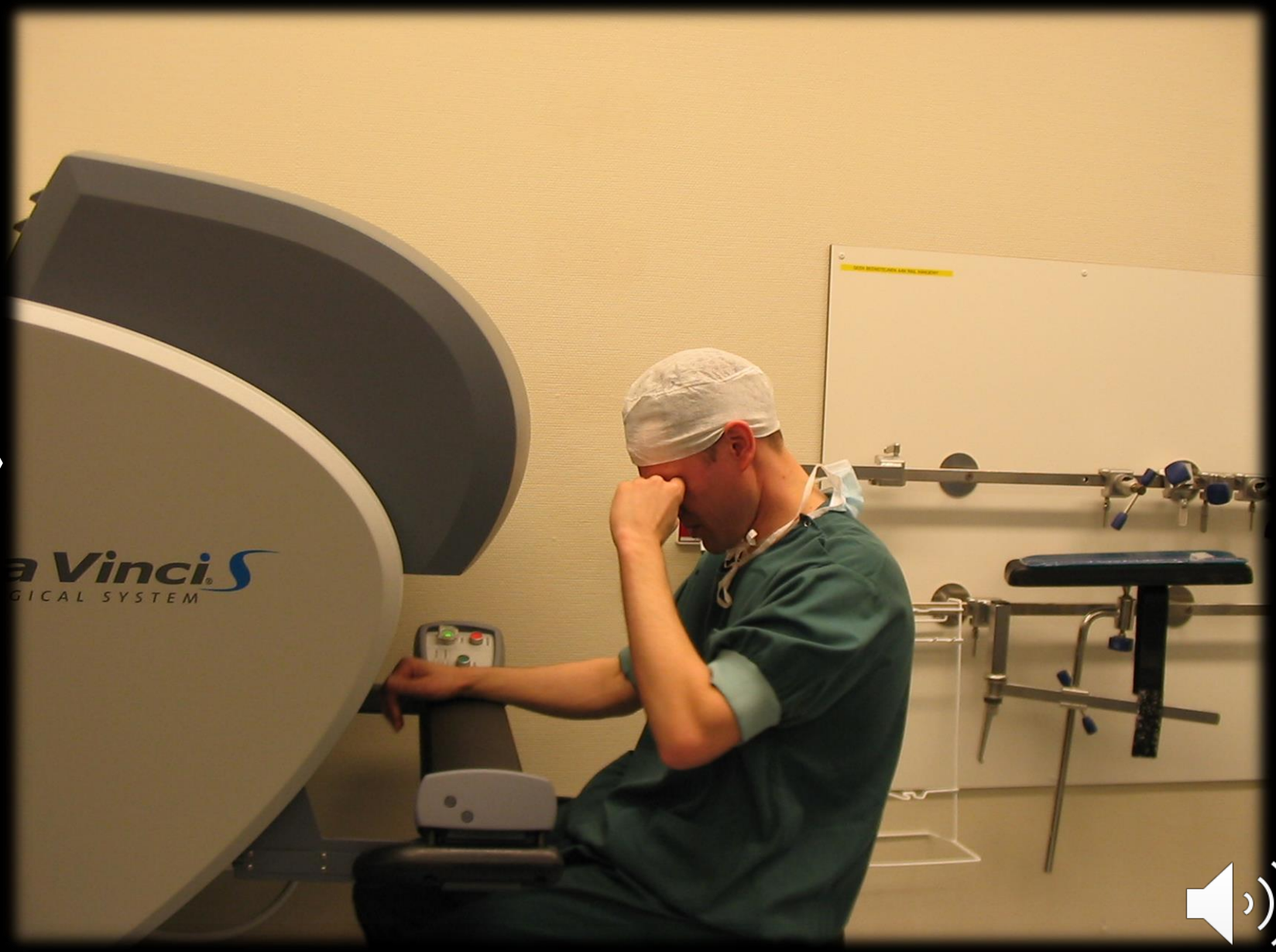




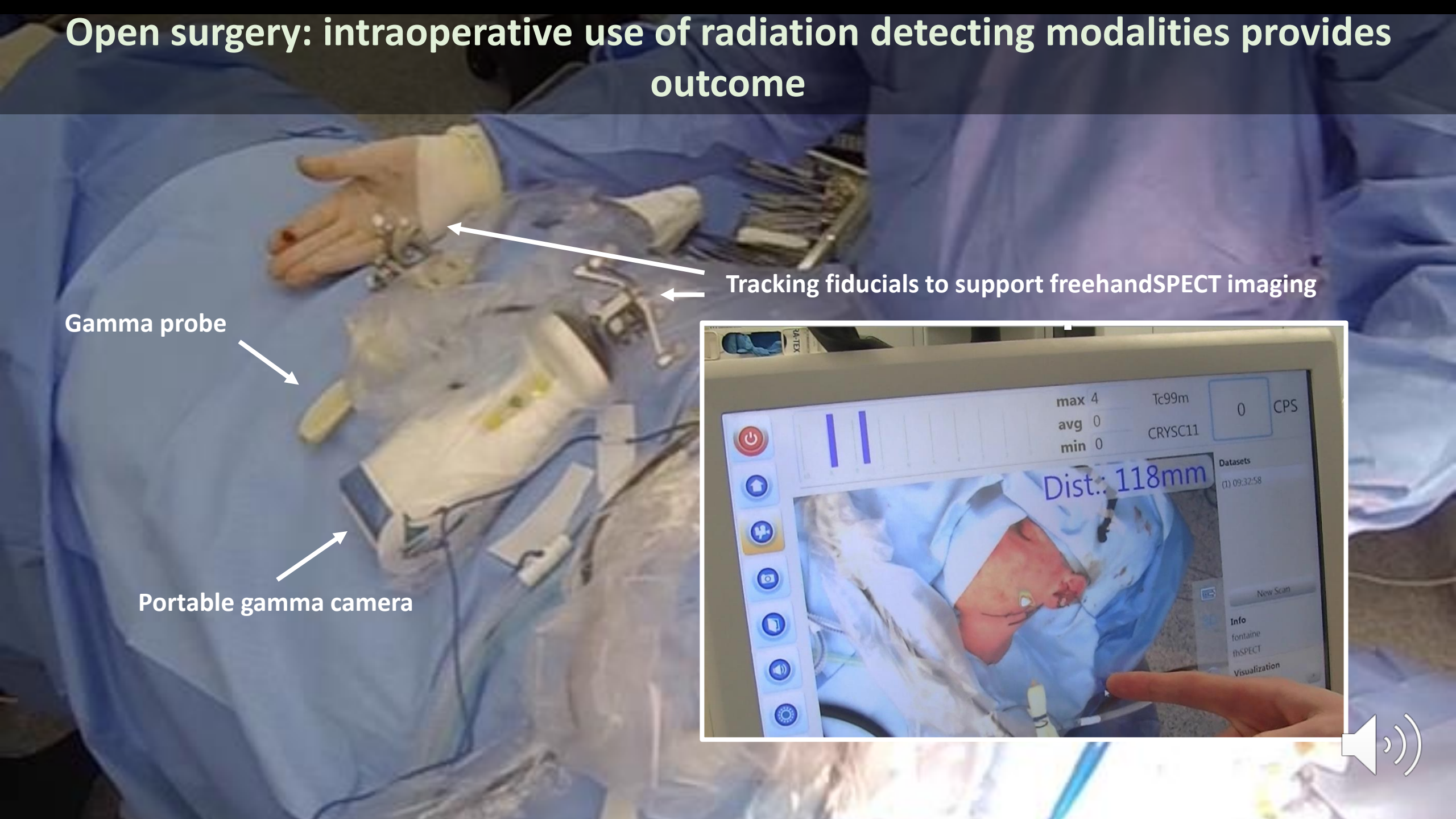
Hensbergen et al JNM 2019; patent pending

Technologies- radioguided surgery

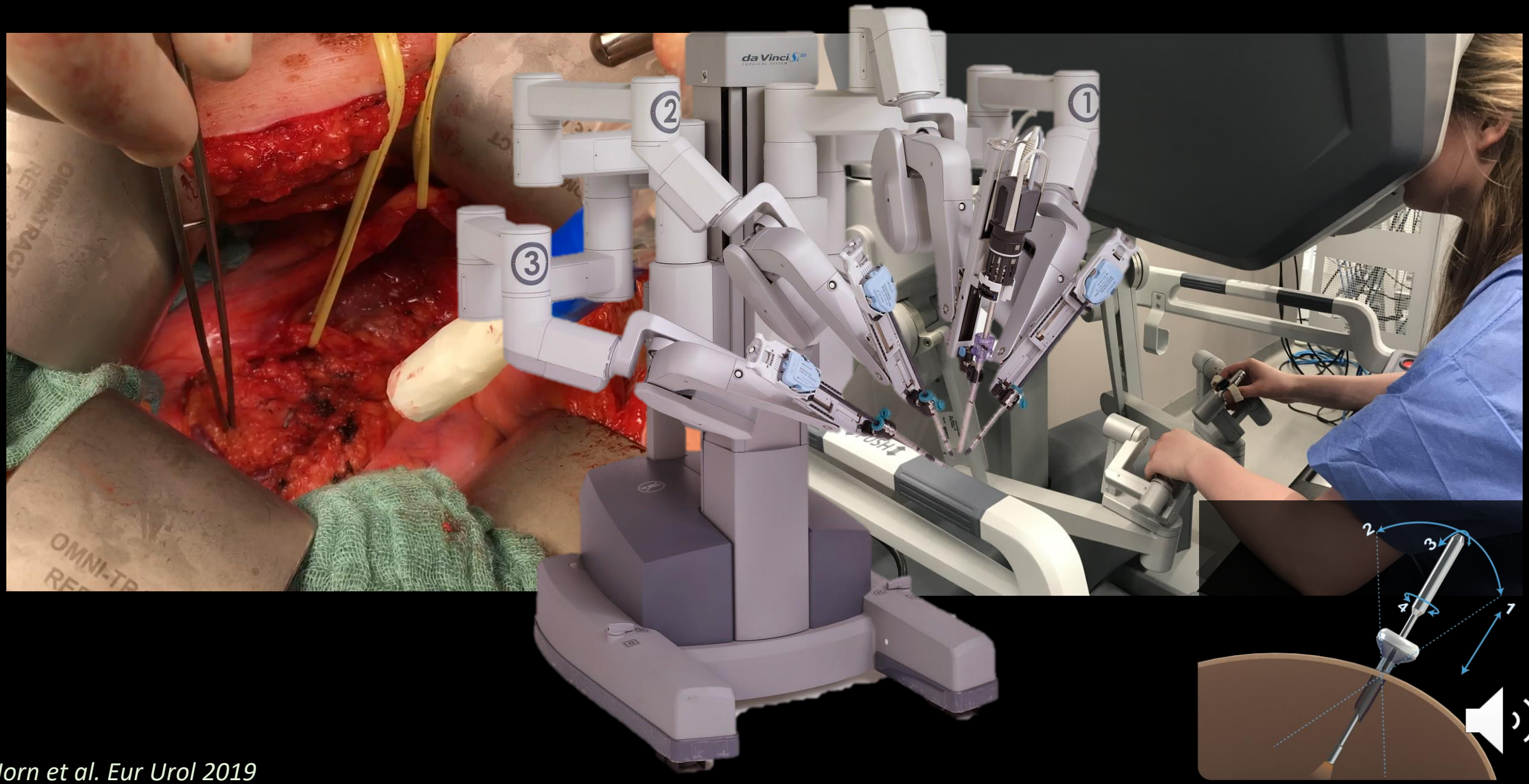
How can we translate imaging at nuclear medicine to the OR?



Open surgery: intraoperative use of radiation detecting modalities provides outcome

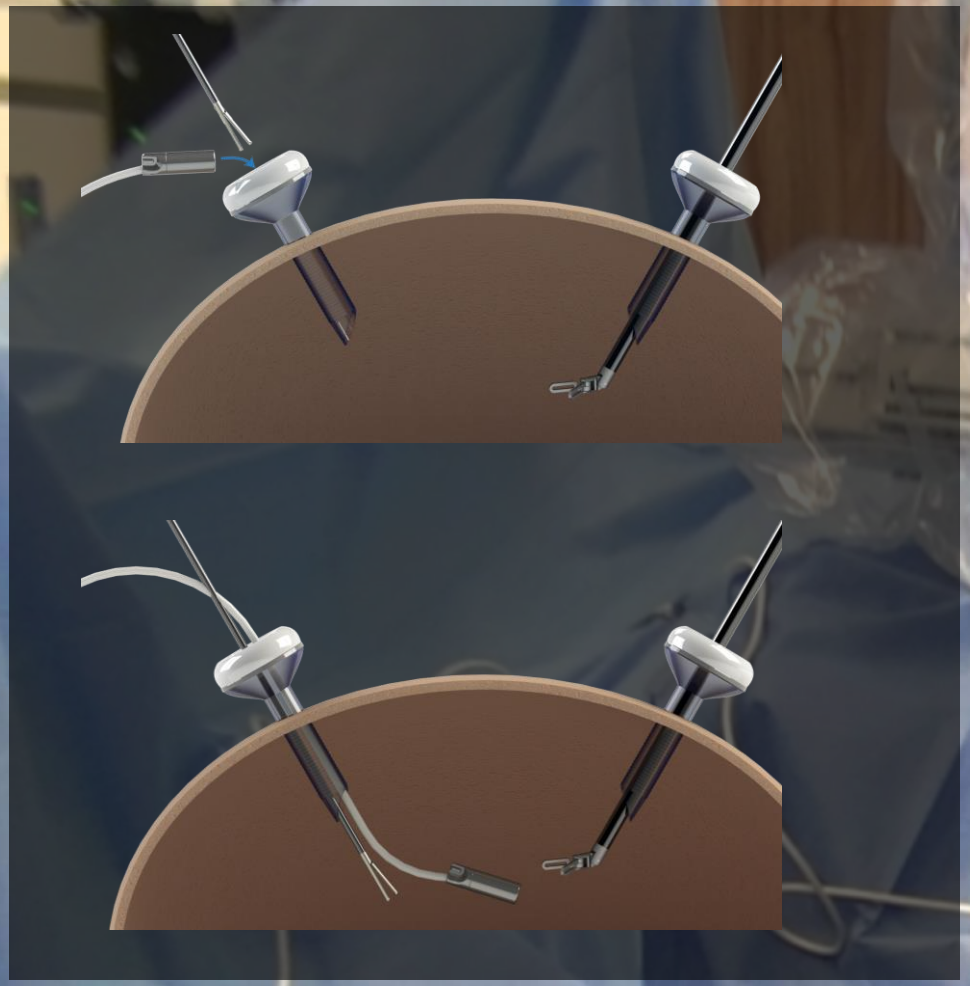


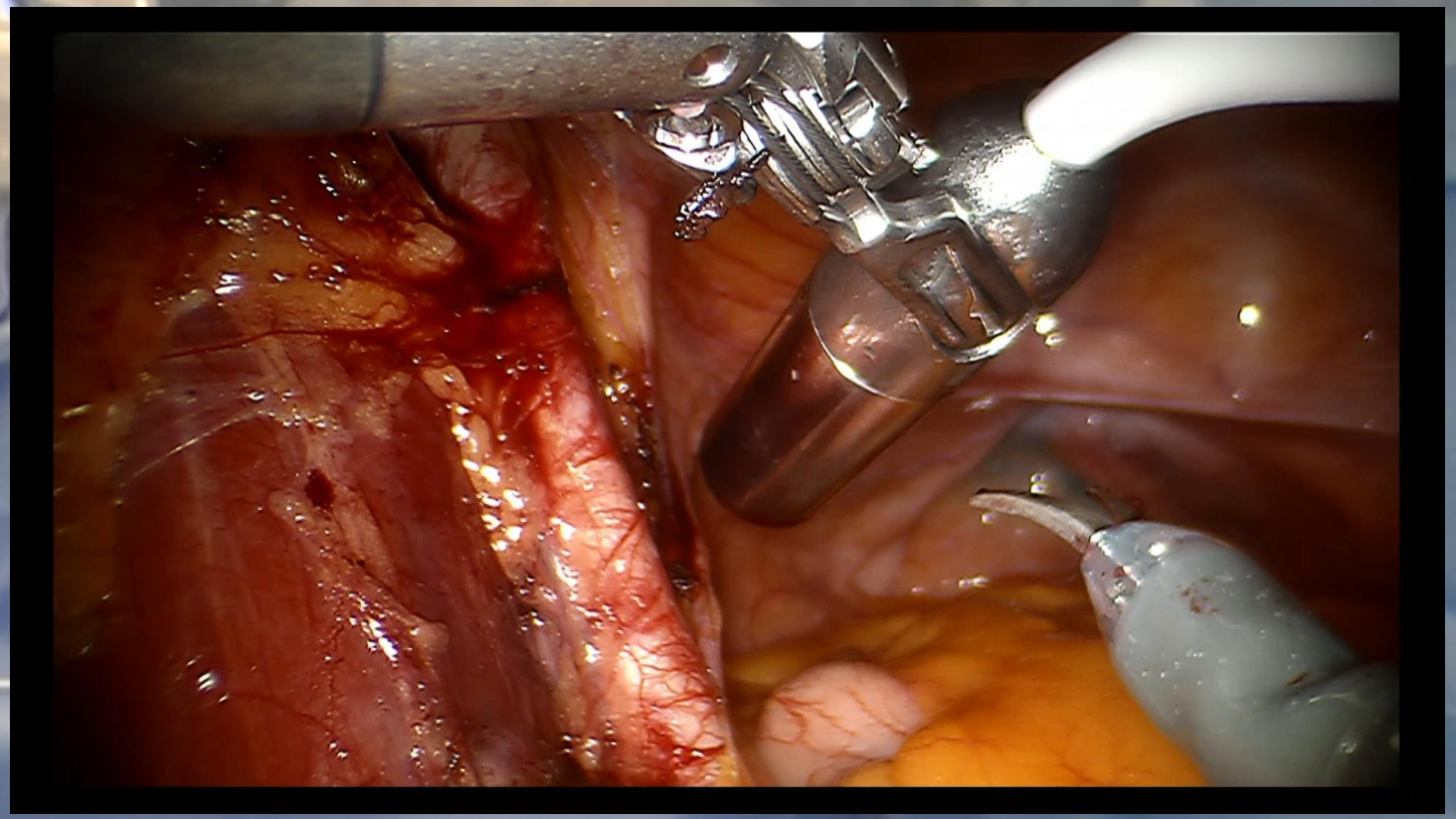
Converting to laparoscopic surgery creates new challenges



Horn et al. Eur Urol 2019

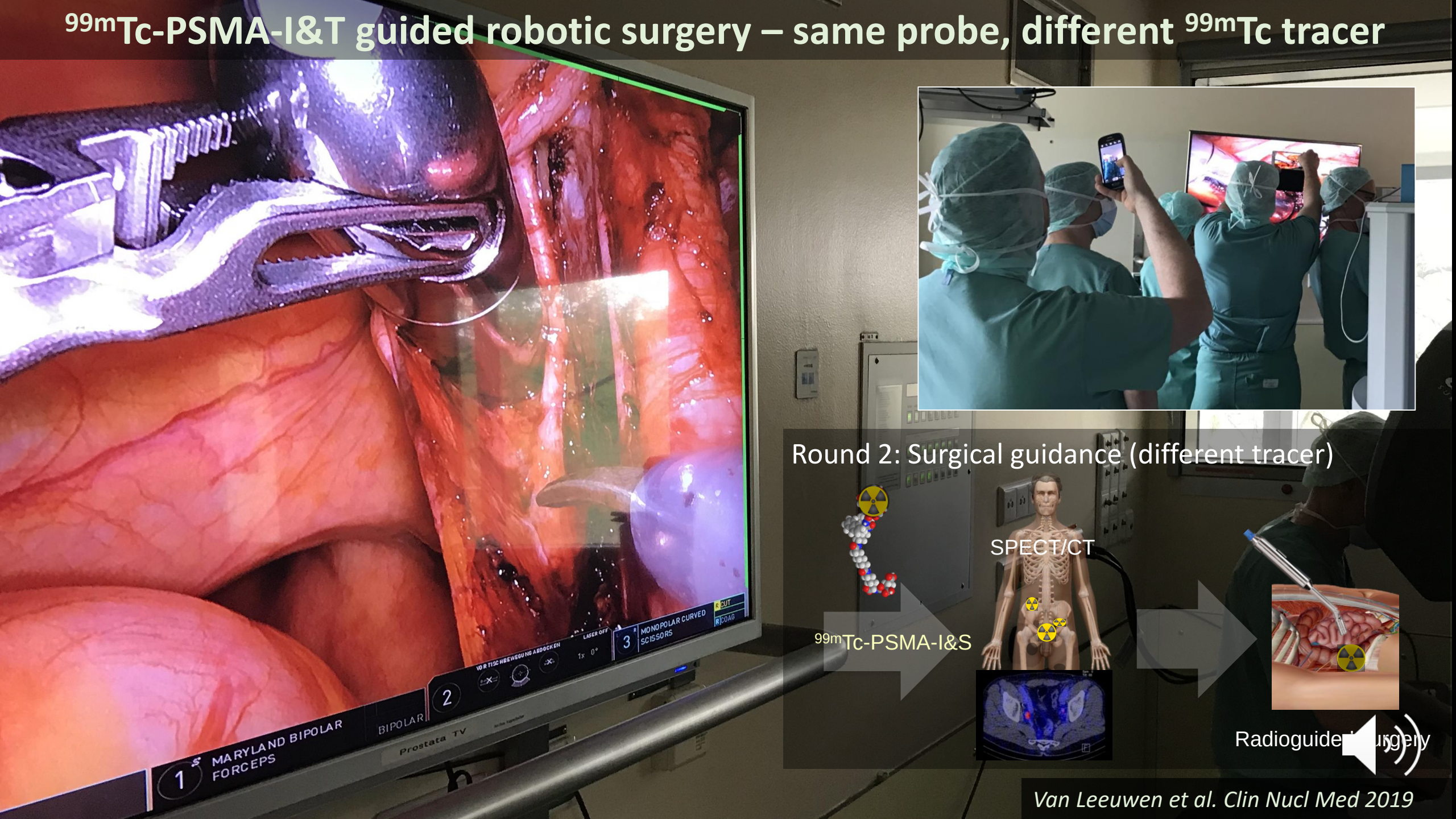
DROP-IN gamma probe to facilitate lymphatic mapping procedures





van Oosterom et al. Am J Nucl Med Mol Imaging 2016, Meershoek et al. EJNMMI 2018

^{99m}Tc-PSMA-I&T guided robotic surgery – same probe, different ^{99m}Tc tracer



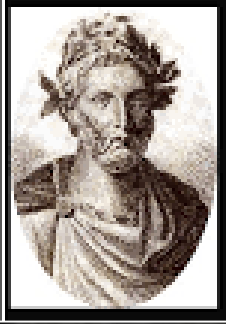
Van Leeuwen et al. Clin Nucl Med 2019

DROP-IN beta probe, expanding the concept

Round 2: Surgical guidance (different tracer administration)

Collimatti et al. under revision

Technologies- fluorescence guided surgery



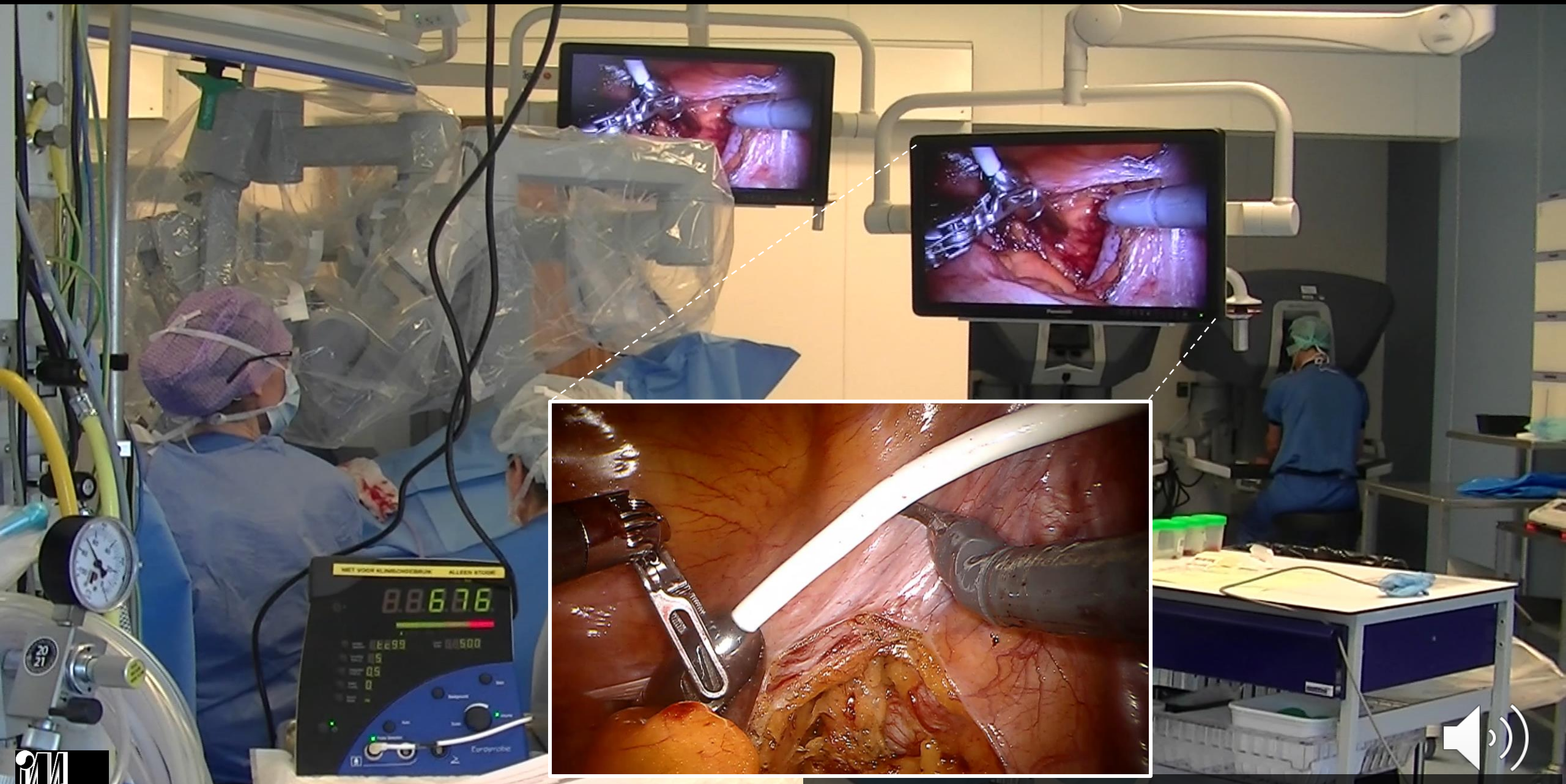
One eye-witness weighs more than ten hearsays —
Seeing is believing all the world over.

(Plautus)

Real-time lesion identification in anatomical context

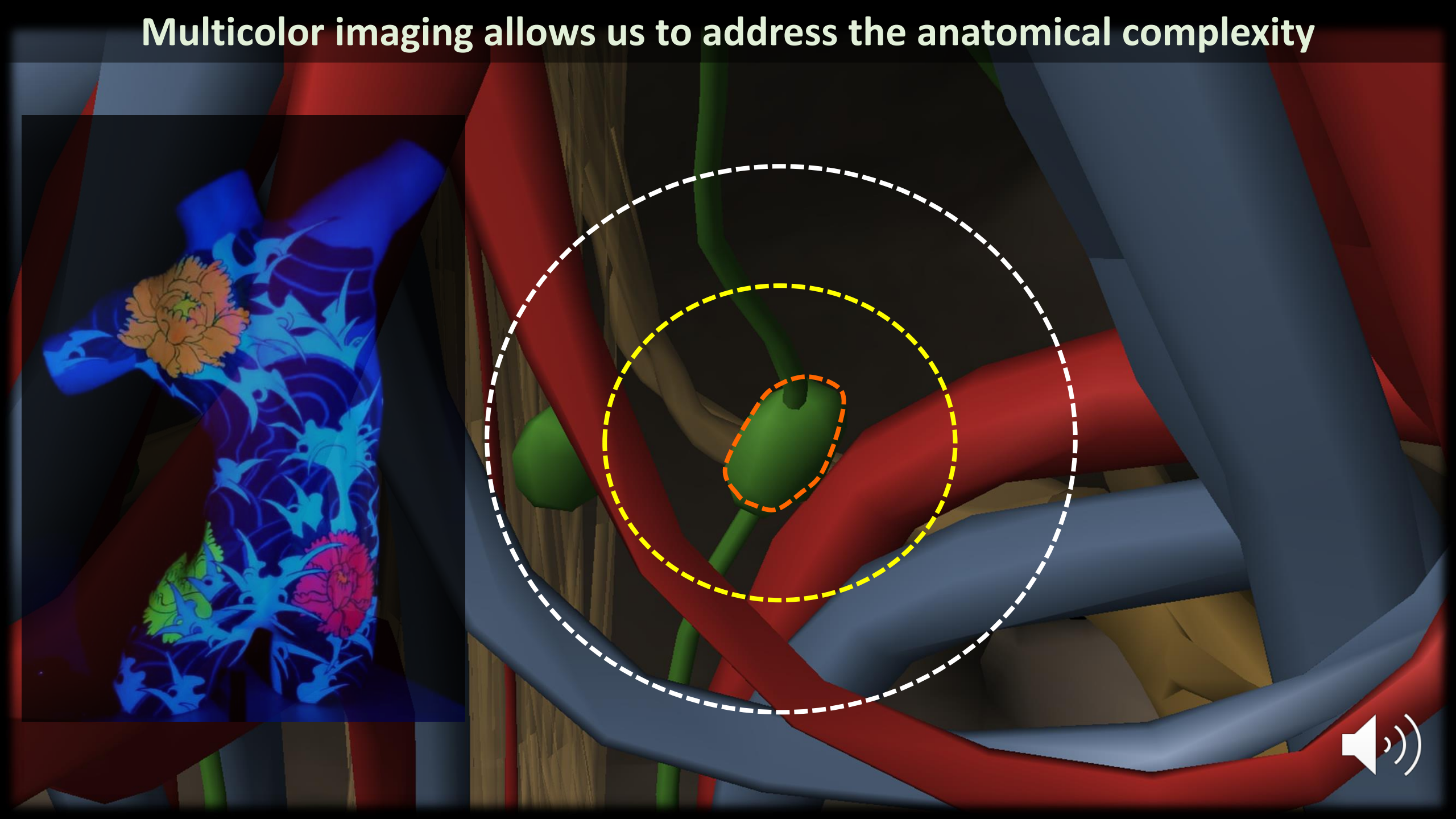
Vd Berg et al., *Annals of Surgical Oncology* **2016**

With hybrid tracers radio- and fluorescence guided surgery work together

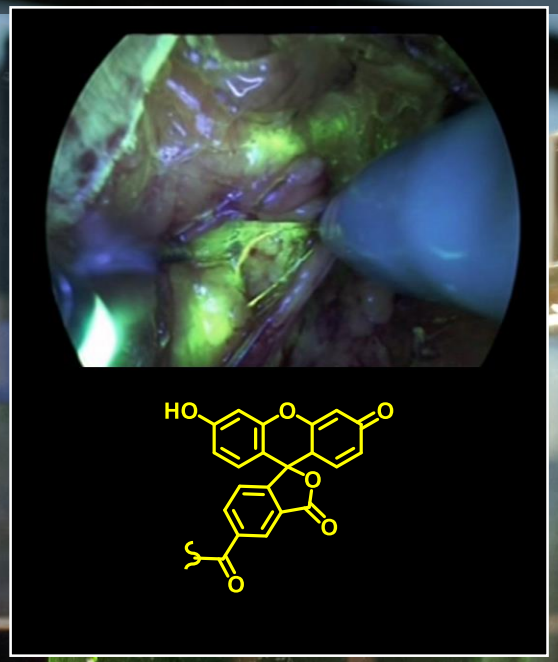


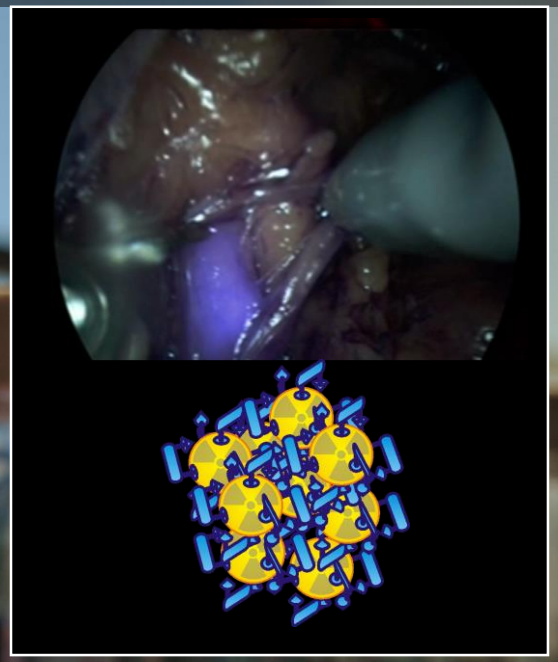
Meershoek et al. Eur J Nucl Med Mol Imaging 2018

Multicolor imaging allows us to address the anatomical complexity



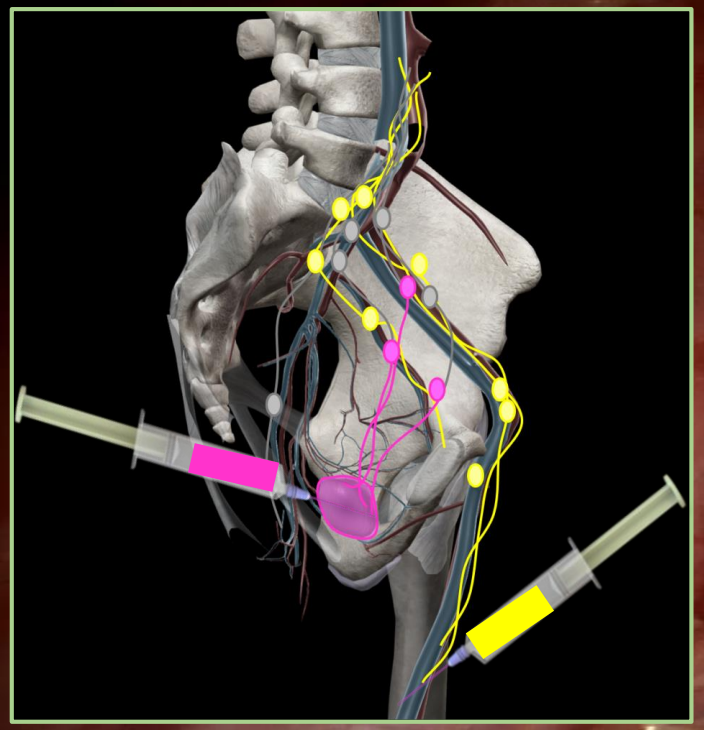
This is made possible by using differently colored tracers for different targets





Van den Berg et al, *Eur Urol* ***2016***

Intraoperative differentiation between key features can help reduce surgical morbidity



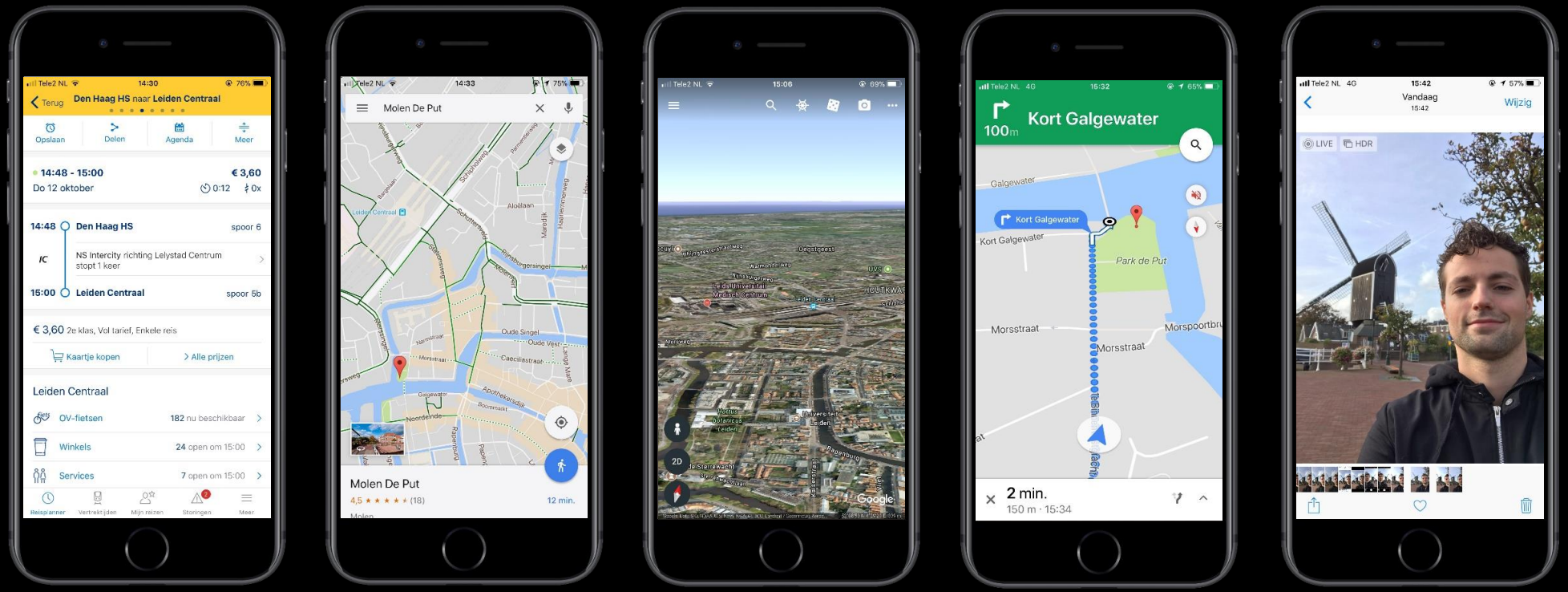
Meershoek et al. *J Nucl Med* **2018**

Identifying primary tumor margins while allowing with lymphatic mapping

Martijn et et al. manuscript in preparation

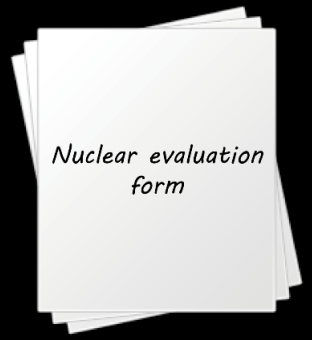
‘GPS-like” navigation

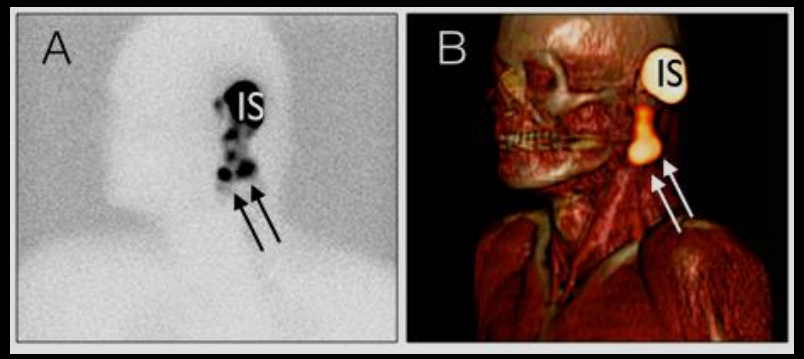
Navigating surgical tools in preoperative roadmaps, connecting the dots



Preoperative imaging

intraoperative imaging





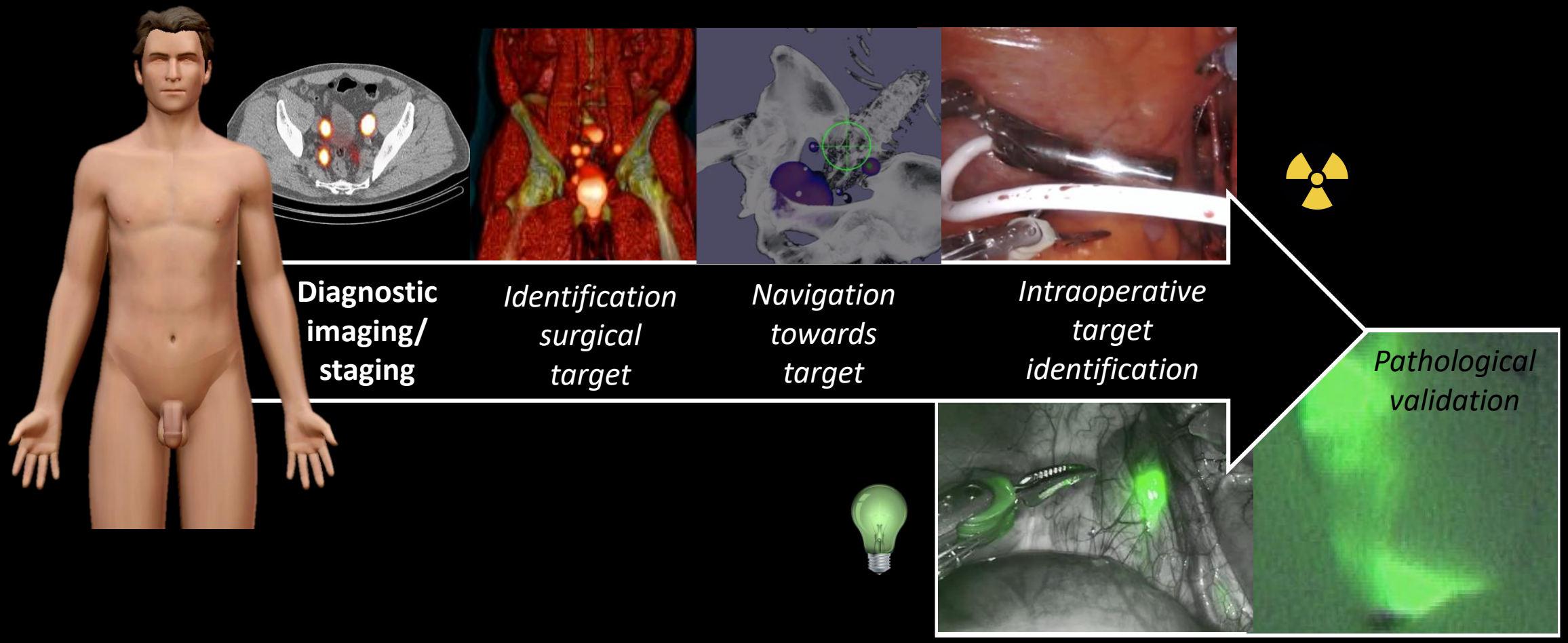
Van Oosterom et al. Current Opinion Urol 2018

Registering preoperative images to the patient

First clinical implementation studies promising, but intraoperative imaging remains imperative to confirm the target location

Van Oosterom et al J Bio Opt 2018

Conclusion: integrating technologies helps advance image guided surgery



Acknowledgements

CORPUS reis door de mens
INTUITIVE SURGICAL
HAMAMATSU PHOTON IS OUR BUSINESS
SURGICeye
STORZ KARL STORZ — ENDOSKOPE
ORSI ACADEMY
Crystal Photonics
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NWO Veni, Vidi, Vici
NKI-AVL
LUMC
TUM
SAPIENZA UNIVERSITÀ DI ROMA
Universitätsklinikum Essen
WAGENINGEN UR For quality of life
OSPEDALE SAN RAFFAELE
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