Interventional Molecular Imaging – a hybrid approach

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www.interventionalmolecularimaging.com

Interventional Molecular Imaging Laboratory

'From Molecule To Man'

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The surgical theatre provides a setting were sometimes simple things become complex..



..so complex situations need to be unraveled and accompanied with practical solutions



Anatomical Imaging

Functional







US



Modalities for in-depth imaging



Molecular Imaging





Gamma imaging









Modalities for superficial imaging

Imaging modalities



Fluorescence in context of gamma-emissions



Radioactivity

Radiometals e.g. 99m Tc or 111 In Half-life (t_{1/2}) Emission energy (keV) Emission

Emissions and penetration depth



Integration of nuclear medicine and fluorescence guidance to generate a "best of both worlds" hybrid scenario

Nuclear medicine vs. Fluorescence imaging

Maurits Escher

⊻~44 11113

Quote: "researchers with new concepts are like salmon that swim against the stream"



Challenge: don't get eaten..



Aim:

Initiate clinical proof of concept trials with hybrid or bimodal tracers to

- 1) Proof the concept adds clinical value;
- 2) Optimize logistics and engineer matching modalities;
- 3) Provide a platform for technology dissemination into tumor receptor targeted applications.

sentinel node resections during robot assisted surgery (technology aimed at identifying micro metastases)



Extensive surgical exploration for signal that may, or may not be present is likely to do more harm than good

Sentinel node concept = interrogating the lymphatic plumbing of the tumor

band, fill

PLANNED TO PERFECTION

Top Yorkshire wedding planner Emma Marygold, who was the creative genius behind the wedding of Olympic gold medallist Jessica Ennis last year, explains the new trends for 2014.

pics | Marygold Wedding Planning

Ar

EN

Every

IS

Weddings are my true passion and my inspiration comes from all around me; and by keeping up to date with fashion, interior design, the latest movies and event trends, here is a taste of what I expect to see on the wedding scene over the next 12 months. The pales and nude hues are back. Soft, pale and pastels have been impact with text faux furs. This year is all chintz and shint floral patterned funky florals with s Transparency candelabras and trans Flower of choice for Tree Peony. Arrangemen dramatic. Be prepared to from the ceiling, dramat cubes. Include vibrant fr and a mass of green foliage Baby's breath - or gypsop in a mass of giant cloud the ceiling and adorn archit which will be huge in 2014 Lighting is always key s and fairy lights, but also

SN's: the first tum of the differently, a long line of draining lymph live y or hangin nodes

ist-have, although the style continues, s will be added in abundance, frilis, rersized icing flowers and dramatic

> see a new style of Art Cakes, created with hand painted designs, enord to eat!

ery plays an important of ne the moment your open their invitations, its year, good things a small packages, forget oversized invitation, small and dashty

To add fun and design to your apporting to some easier have been super-sized this year and the better! Silver service is out and social perment your chosen

interactive culinary delight ferment luxury with gilded china and seen sate the laws of two funky with coppers and woods are the bringing together of family and funky with coppers and woods are the bringing together of family and

but percentations We set the tread earlier text was for leasting tone-bills water, the texts was a taxoning. Monipue theils for texts with host foldowneds in a very pile pile We had foldown patients of groupshile comming leasting and treas adorest was

manthly but then be been the loss and young grants has been by the heat had but's have it. Change it it

ICG-^{99m}Tc-nanocolloid - a multimodal nanoparticle for the sentinel node procedure based on simple supramolecular chemistry

"standard" in Europe





ICG ICG-99mTc-nanocolloid





GE Healthcare

Concept design 2007, first patient 2009!



Radioguided surgery

Maurits Escher

Sentinel node procedures in the pelvis (technology aimed at identifying micro metastases)

Sentinel node procedures in the pelvis

99mTc-nanocolloid: Long retention (> 30h after tracer administration)

Translation of preoperative images to the intraoperative setting can be complex

ALM

Fluorescence imaging can help provide real-time feedback during surgical interventions



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

Radioguided-surgery: Gamma tracing using a laparoscopic gamma probe



Detection gamma-emission radioisotope

van der Berg et al., Eur J Nucl Med Mol Imaging 2015

Radioguided-surgery 2.0: Gamma tracing using a drop-in gamma probe









Van Oosterom et al. AJNMMI 2016





Radioguided surgery + fluorescence guided surgery

Laparoscopic fluorescence camera





KleinJan et al Eur Urol 2014

Fluorescence provides a high level of detail



Real life surgical guidance with anatomical context!

KleinJan et al., Eur Urol 2014



Started as a novel concept, now a widely accepted technology that has changed medical care

En challenge: integrate different technologies in a single modality







Fluorence nce camera



First clinical grade hybrid modality: the Opto-Nuclear probe



Van den Berg et al., EJNMMI 2015

EURORAD- new product

Opto-nuclear probe in vivo



Gamma tracing in combination with optical imaging





KleinJan et al., JNM 2016

EURORAD, Oncoviosn, Karl Storz Endoscope- prototypes

Comparison sensitivities hybrid modalities



In the end a combination of complementary (and fully integrated) guidance features helps provide the most accurate guidance



What is still missing is the visual presentation of different features

Image guided surgery technologies evolve in manner similar to other daily technologies e.g. the directional guidance provided by smart phones



In the end a combination of complementary (and fully integrated) guidance features is most likely to provide accurate guidance.

SPECT/CT based augmented reality as reference for navigation





KleinJan et al JNM 2016

Brouwer et al *BJU* **2014**

Requirement 1: complementary tracers



SN identification

Lymphangiography

Two color imaging (multiplexing)

Near-infrared





Fluorescein





ICG-99mTc-nanocolloid



Van den Berg et al, Eur Urol 2016

Can the hybrid concept also be of value for tumor receptor targeted applications?



Effectively applied on:

Peptides, Proteins, nanobodies, mAbs, viruses, nanoparticles, etc.

Various tumor markers can be targeted in a preclinical setting:

Her2, CXCR4, <u>PSMA</u>, sst, $\alpha_V \beta_3$ -integrin, C-Met, uPAR, CEA, etc.

In the preclinical setting the radiolabel helps during the evaluation of the pharmacokinetics

Welling et al Biocojugate Chem 2015, Bunschoten et al. Bioconjugate Chem 2016 etc. etc.



Chemistry

Targeting the Prostate Specific Membrane Antigen (PSMA)



Challenge: to create PSMA tracers with optimal properties



Validation of a hybrid PSMA tracer in vitro

Preclinical validation of a hybrid PSMA tracer in vivo



Next step include nerve imaging



The true potential of precision medicine not only lies in ensure cure of the disease, but also preserving a maximal quality of live for the patient.



Conclusion: Translational research can generate many possibilities, but also relies on strong interaction between the various disciplines involved

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