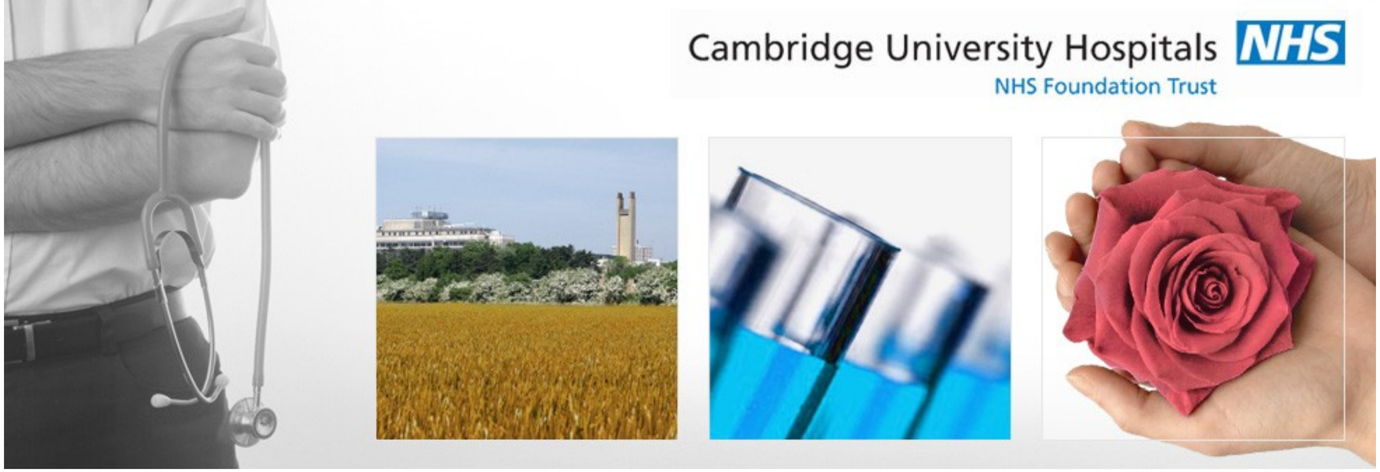

New areas of research using functional imaging in cancer

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Introduction

- Review areas of current research beyond PET in molecular imaging of cancer
- PET-MR
- Hyperpolorised MR
- Optical imaging
- Photoacoustic imaging
- Ramen imaging
- Cerenkov radiation

PET/MR

- The latest thing
- Is this the best thing
- Is this the future of Nuclear Medicine
- Should I get a PET/MR
- What will I use it for

Looking for the killer indication

- Maybe look for ever
- However, some areas where MRI better than CT
- Pelvic tumours
- The liver
- The brain
- Also children to reduce radiation dose

Getting a PET MR

Buy an Apple computer

Download Osiris

Upload PET

Upload MR

A real PET/MR

- Number 1 problem
- PMT tubes are very sensitive to magnetic fields
- The PET detector would need to be RF shielded
- Different engineering solutions

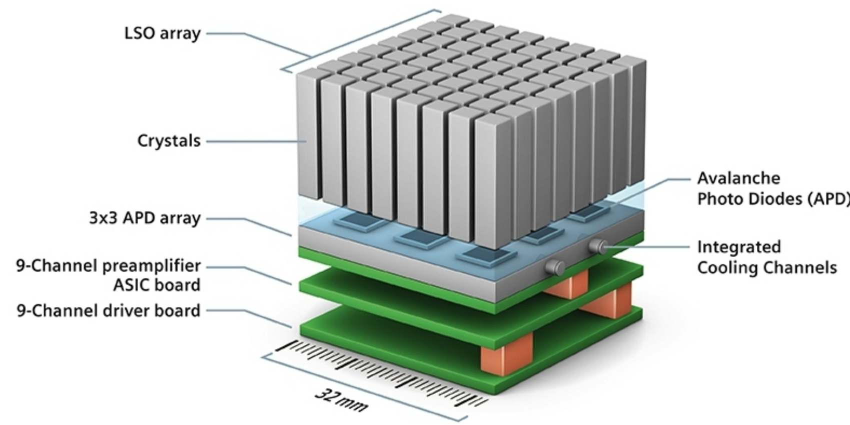
The GE solution 1

The Philips solution

The Siemens solution

The new PET detectors

- Uses Avalanche Photo Detectors
- Not affected by magnetic fields
- Slower so no TOF yet
- However must be kept at about 40c
- Variation of 10c stops them working but APDs produce a lot of heat



GE solution 2

GE detectors

In PET-MR its about compromise

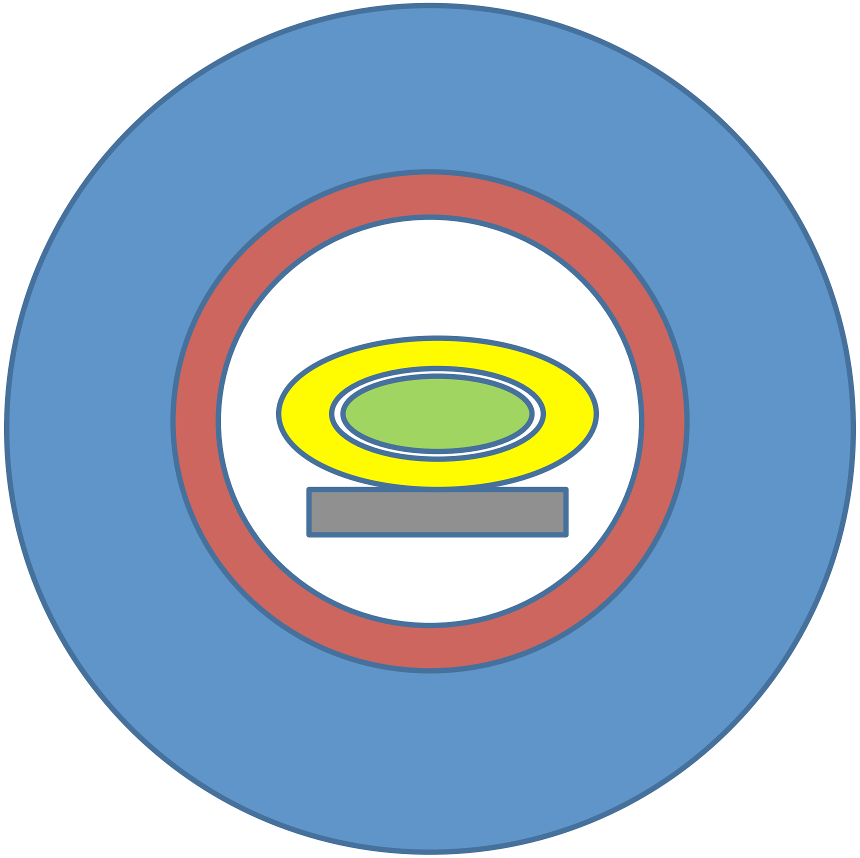
From outside to inside

MRI

PET ring

MRI coil

Patient



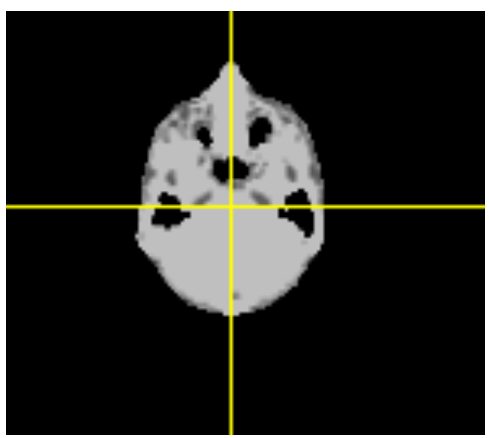
Any other problems

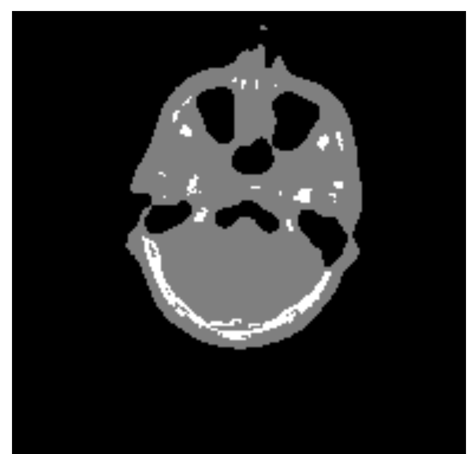
- Just how do you do attenuation correction
- Use attenuation maps bent around body contour on MR
- However MR cannot see bone
- Also MR needs coils all which attenuate
- Good quality MR takes time eg Eyes to thighs PET 20 mins a decent MR about 90mins
- Can we afford that time

PET/MR attenuation correction

- MR based Attenuation Correction is sub-optimal
  - DIXON: Doesn’t distinguish bone – Make as soft tissue
  - UTE: Does see some bone – still struggles
- Really problematic for Neurological PET/MR
  - Brain surrounded by bone

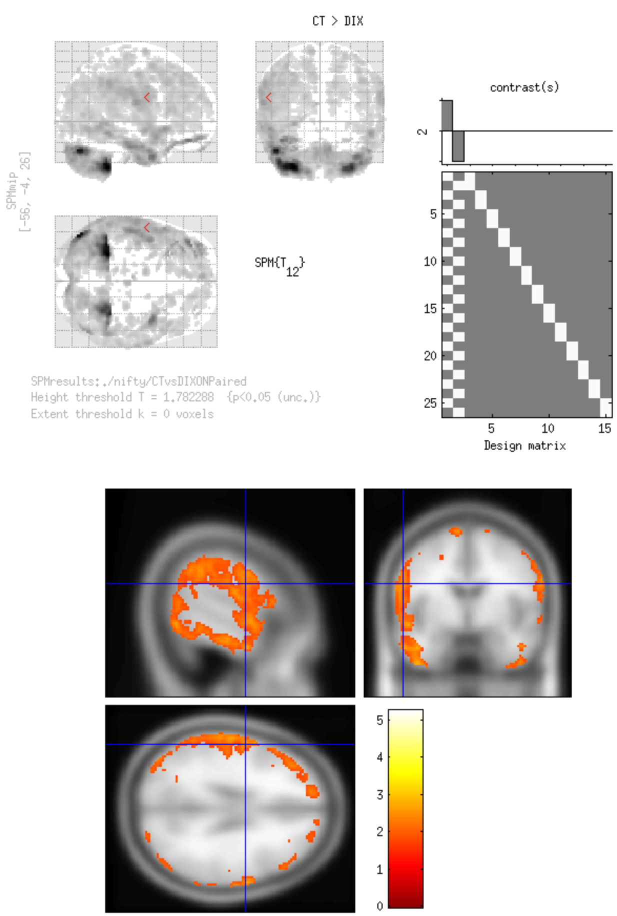
DIXON
AC Map



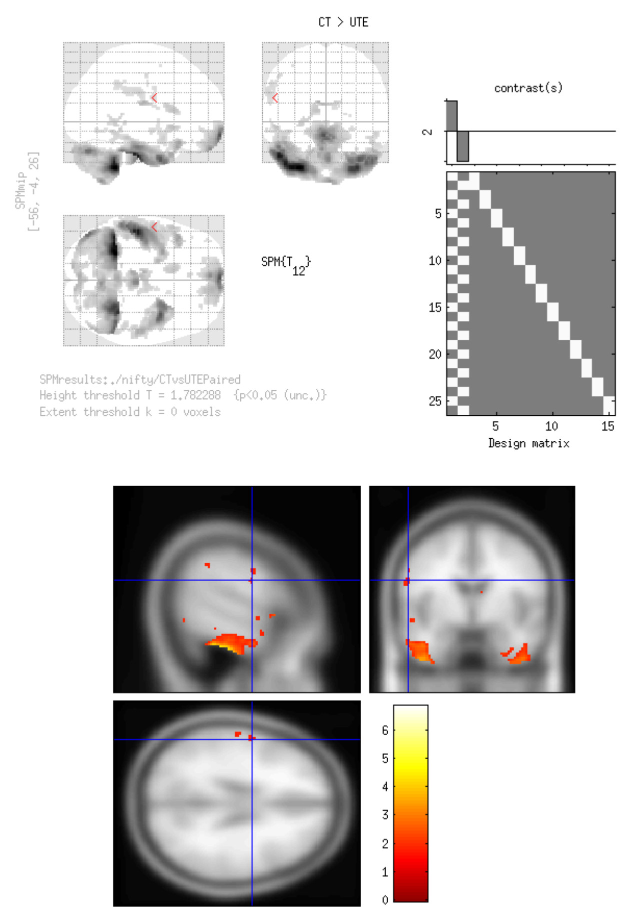


UTE
AC Map

Comparison of CT > DIXON and UTE AC (SUV)



CT vs DIXON



CT vs UTE

CONCLUSIONS

- Current MR based attenuation maps produce artificially reduced uptake in cortical grey matter
- UTE corrections are an improvement over DIXON corrections although there are still problems with complex bone/sinus anatomy.
- SUVR data have similar findings although with the addition of areas of increased PET uptake in sub-cortical areas.

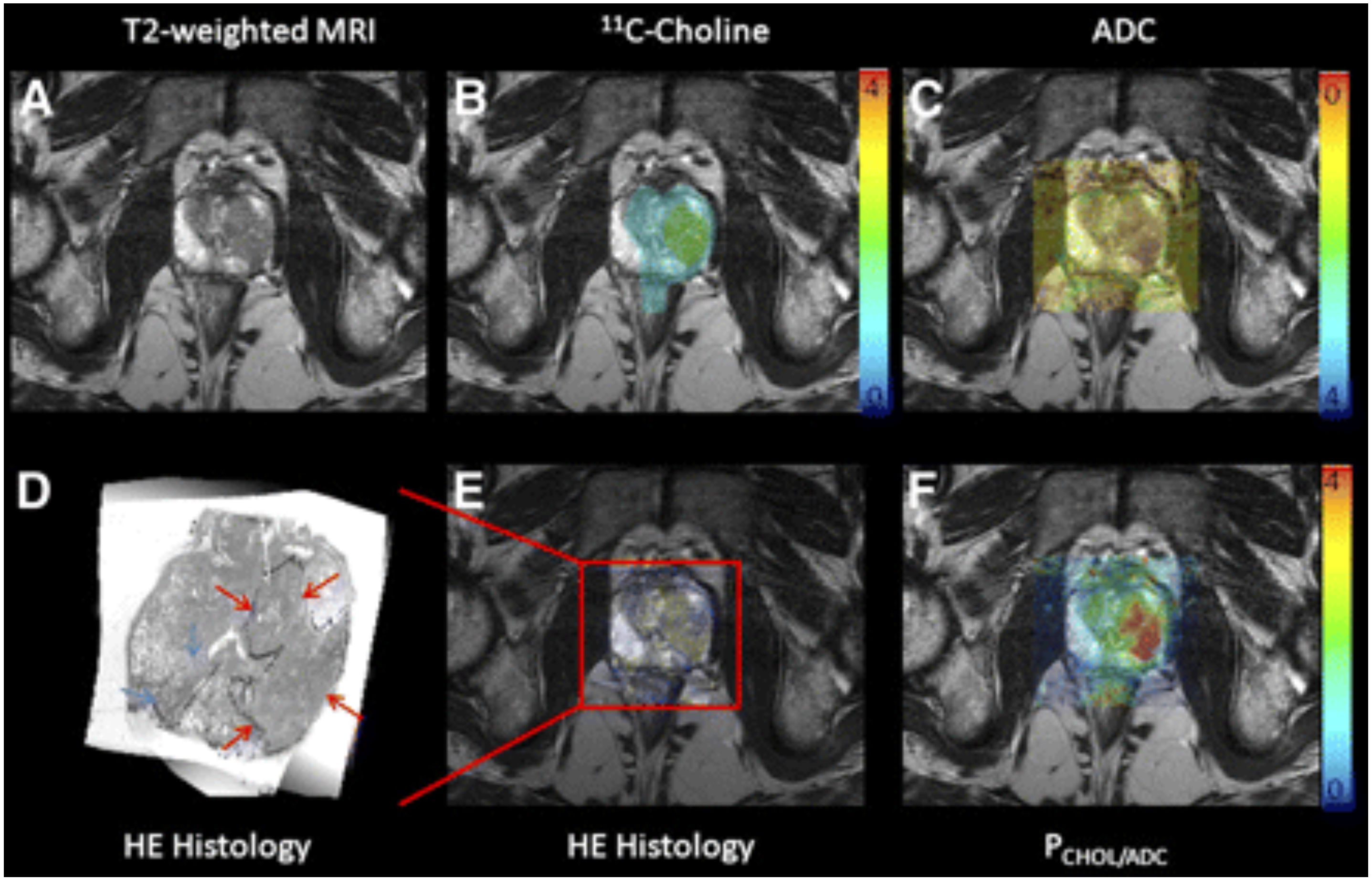
Potential advantages

- Can look at simultaneous MR and PET
- Useful in dementia and cancer research
- APDs very efficient so rad dose less
  - Eg F-18 FDG 400MBq and CT =12mSv
  - F-18 FDG 200MBq and MR =4mSv
- Useful for children and young adults with cancers who need repeat imaging

Does it work

- Park et all JNM 2011
- 17 patients suffering from Ca Prostate PET/MR of the pelvis with C-11 choline
- Good correlation between uptake of C-11 choline and quantitative MR using DWI
- However no technique better than the other

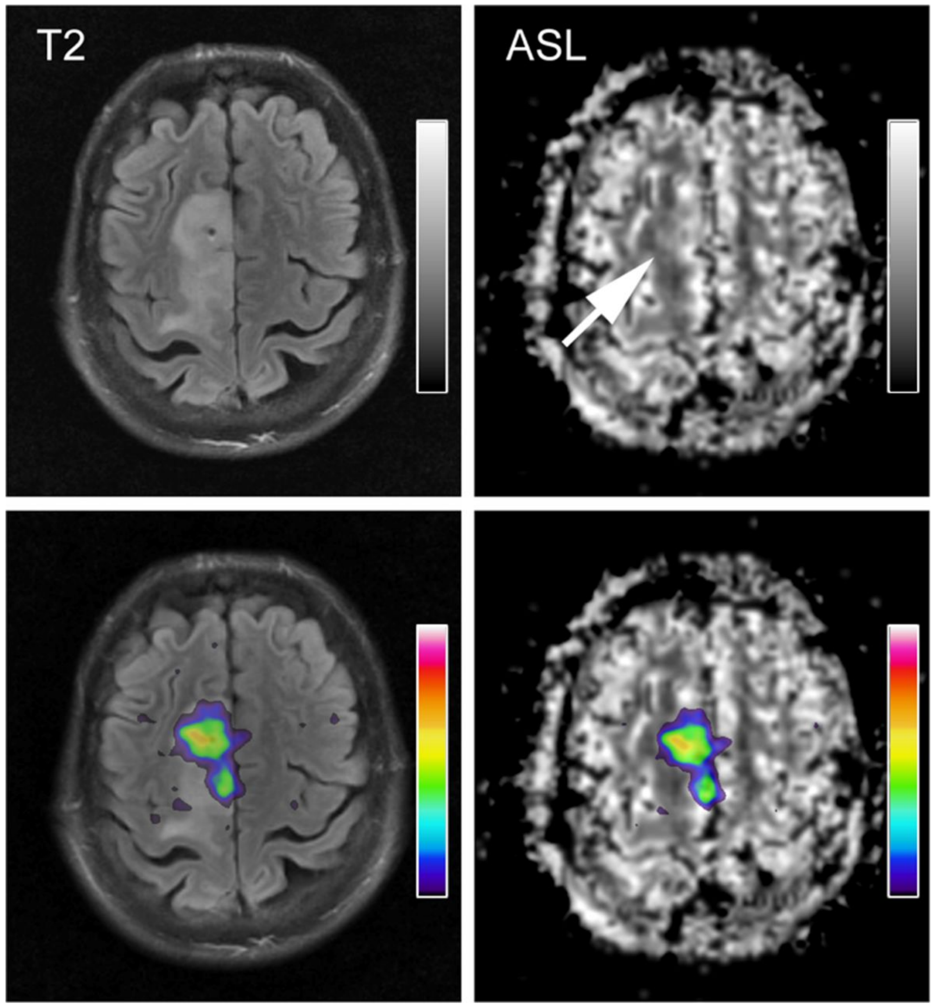
PET-MR in prostate



PET/MR in brain tumours

- Bisdas et al Invest Radio 2013
- MR with spectroscopy fused with simultaneously acquired date from C-11 methionine in 28 patients with pre-treated gliomas
- By combining data could find those areas of the tumours which were most active and directed biopsy

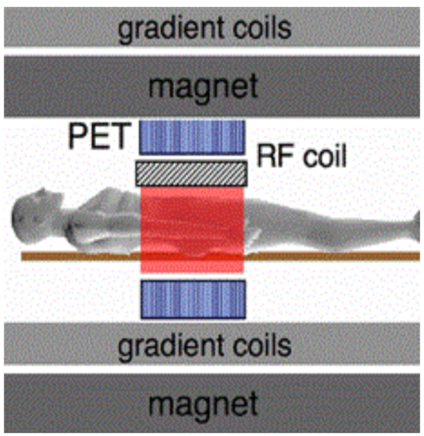
C-11 met PET MR in brain tumour



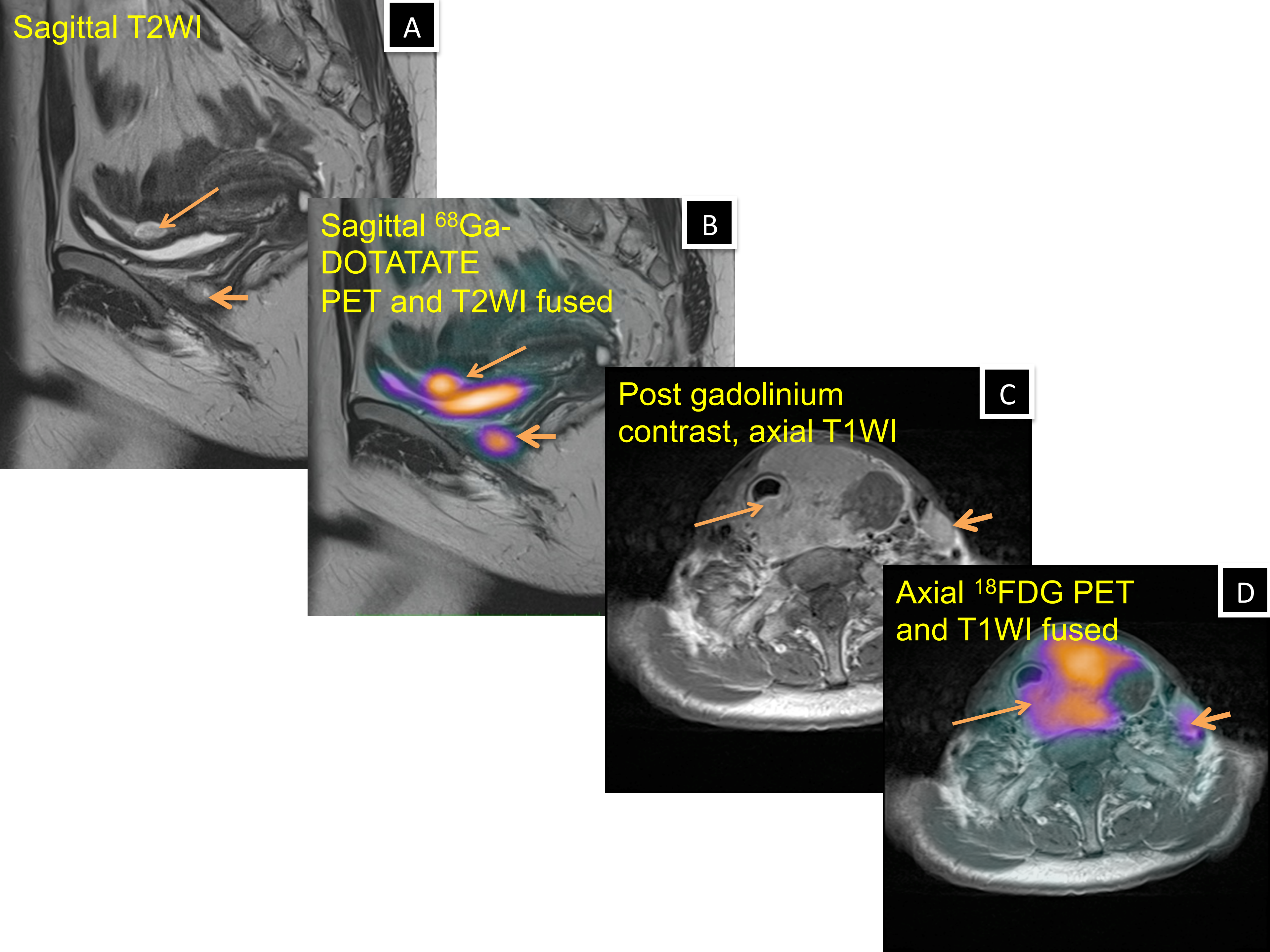
Simultaneous PET/MRI vs PET/CT in Oncological Patients: measured exuberance

K Al-Nabhani, R Syed, J Alkalbani, A Afaq, A Barnes, C O'Meara, R Allie, Z Saad, E panagiotidis, R Sajjan, J Bomanji.

Institute of Nuclear Medicine, University College London Hospitals, UK



Conclusion: Compared to PET/CT, PET/MRI improves disease interpretation in selected cases based on better tissue resolution with management impact in 10%.



Sagittal T2WI
A
Sagittal 68Ga-
DOTATATE
PET and T2WI fused
B
Post gadolinium
contrast, axial T1WI
C
Axial 18FDG PET
and T1WI fused
D

Summary

Aim: Evaluate clinical impact of PET/MRI vs PET/CT in management of patients with known malignancies.

Methodology: 50 patients underwent PET/CT followed by PET/MRI. Primary and non-primary lesions identified. Degree of confidence for anatomical localization and degree of inter-observer agreement was measured. By 3 experienced radiologists and nuclear medicine physicians.

Results:

•PET/MRI identified 227 tracer avid lesions including 10 more primary lesions than those detected by MRI alone.

• Anatomical site was correctly identified in 224/227 lesions (99.1%: 38.8% primary, 61.2% non-primary).

•Overall inter-observer agreement was 97.6% for primary and 95% for non-primary lesions.

•Using PET/MRI, overall confidence in anatomical localization improved by 1.3%.

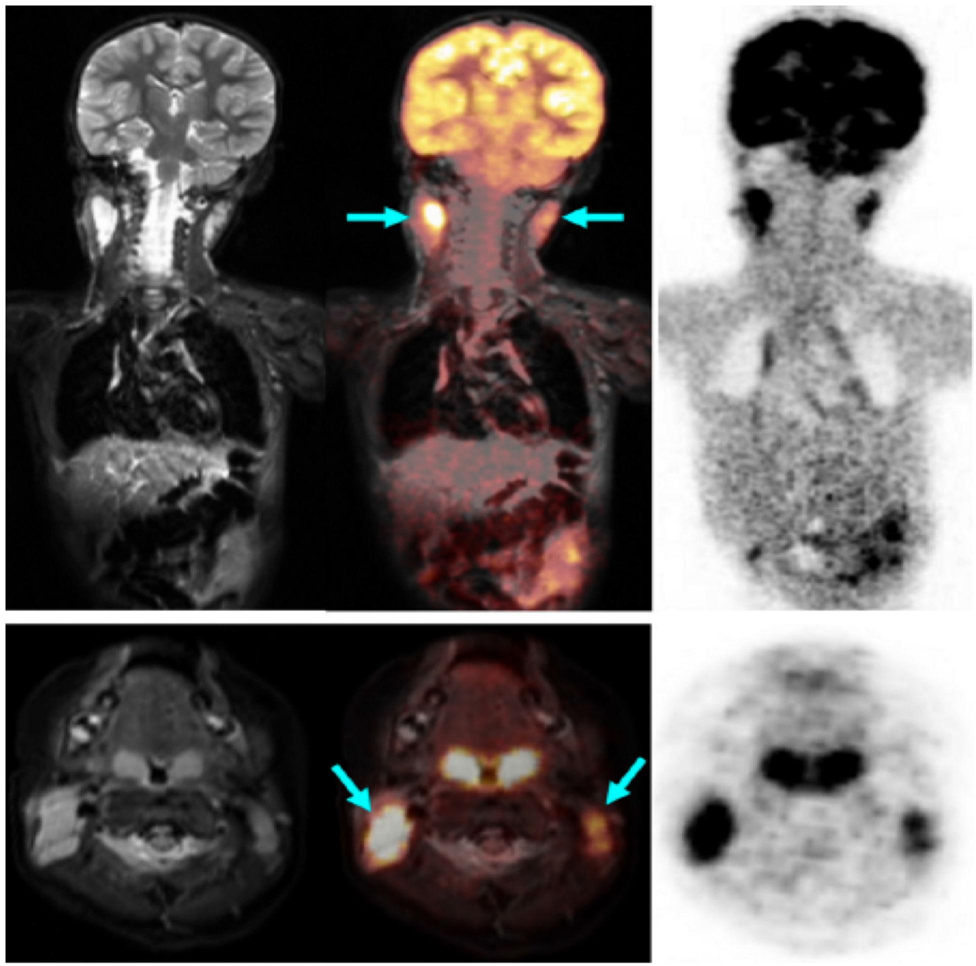
•PET/MRI significantly improved local disease staging by 5.6 % with overall improvement in confidence in assessing disease extent.

Conclusion: Compared to PET/CT, PET/MRI improves disease interpretation in selected cases based on better tissue resolution with management impact in 10%.

PET MR in lymphoma

- Heacock et al New York AJR 2015
- 28 patients with lymphoma imaged with PET/MR
- PET found 100% of all involved nodes MRI DWI found 62%
- MR good for localisation of positive nodes
- Can be used alone as good as PET-CT but lower radiation dose

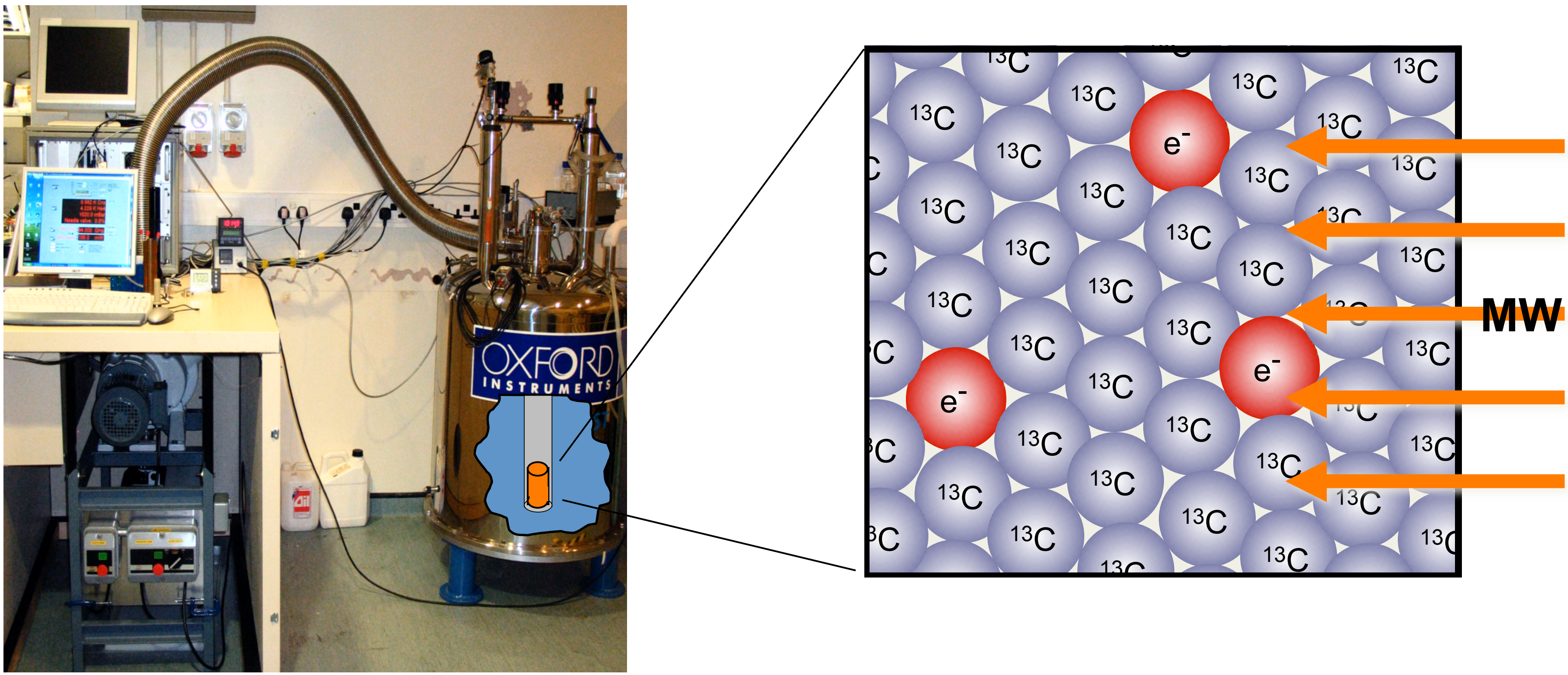
PET/MR of lymphoma in the neck



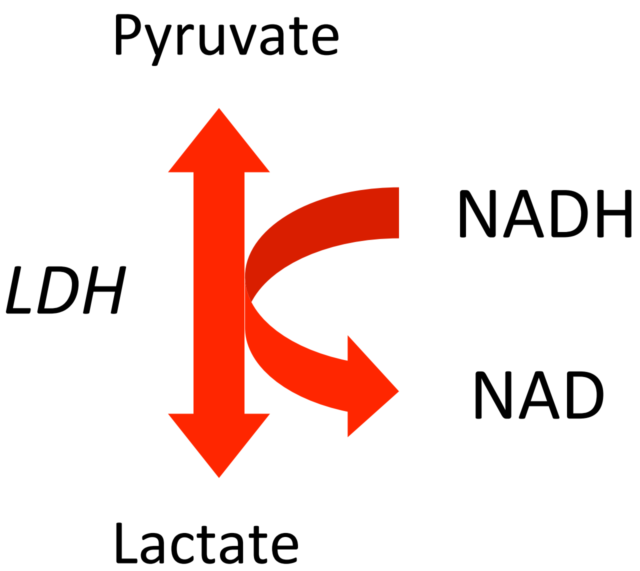
Hyperpolorised MRI

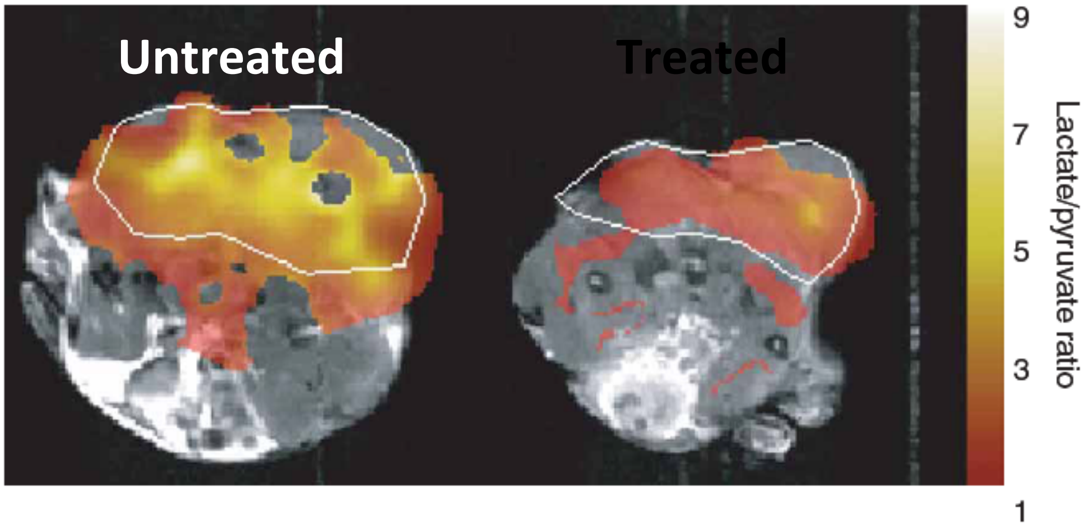
- MR has poor signal pick up
- Need grams of Gd to get signal
- Signal can be amplified by spinning all the atoms in the same direction
- Called hyperporization
- Then need only ng similar to PET
- Can image for a few minutes only

Dynamic Nuclear Polarisation



Imaging enzyme activity

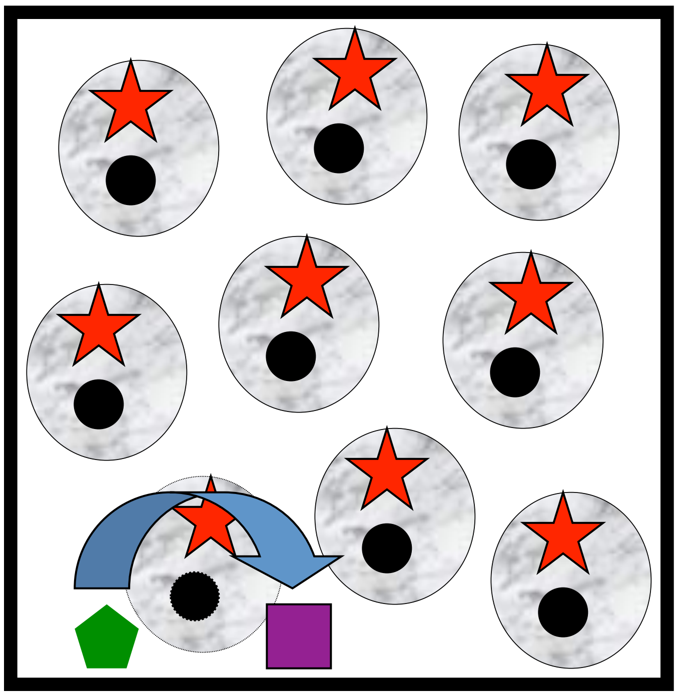


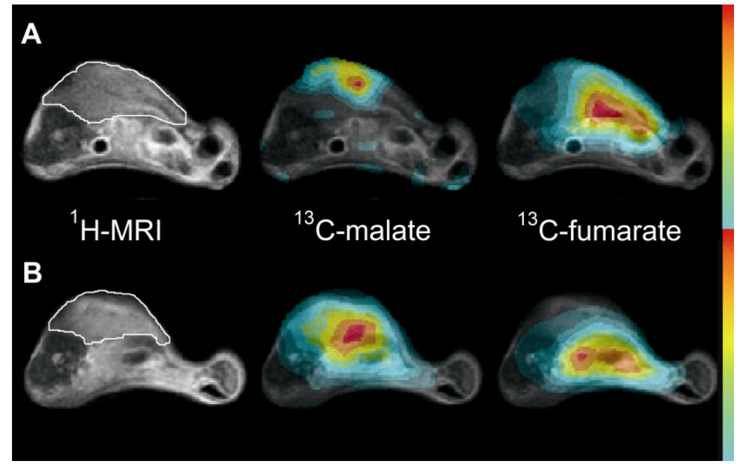


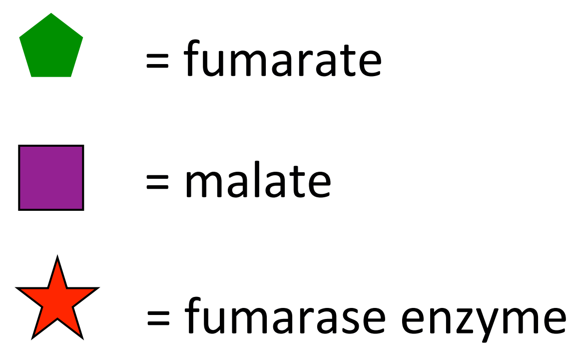
Day *et al.* (2007), *Nature Medicine* 13(11):1382

Imaging cell death

Cell death

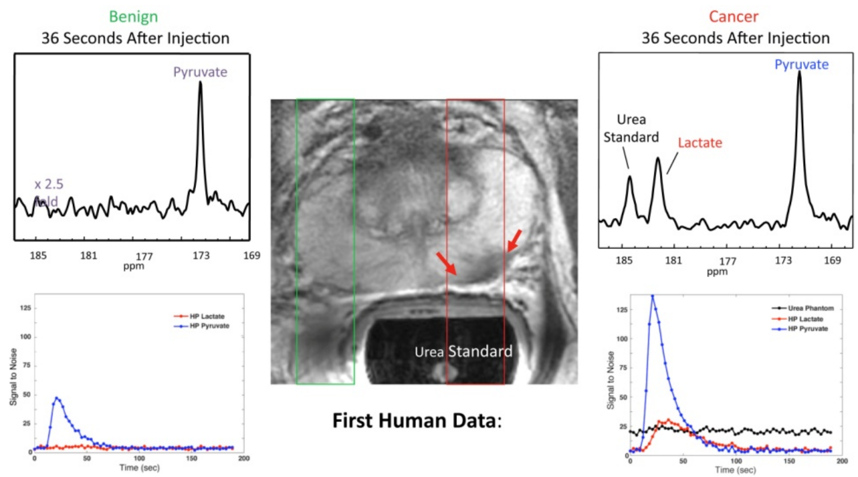


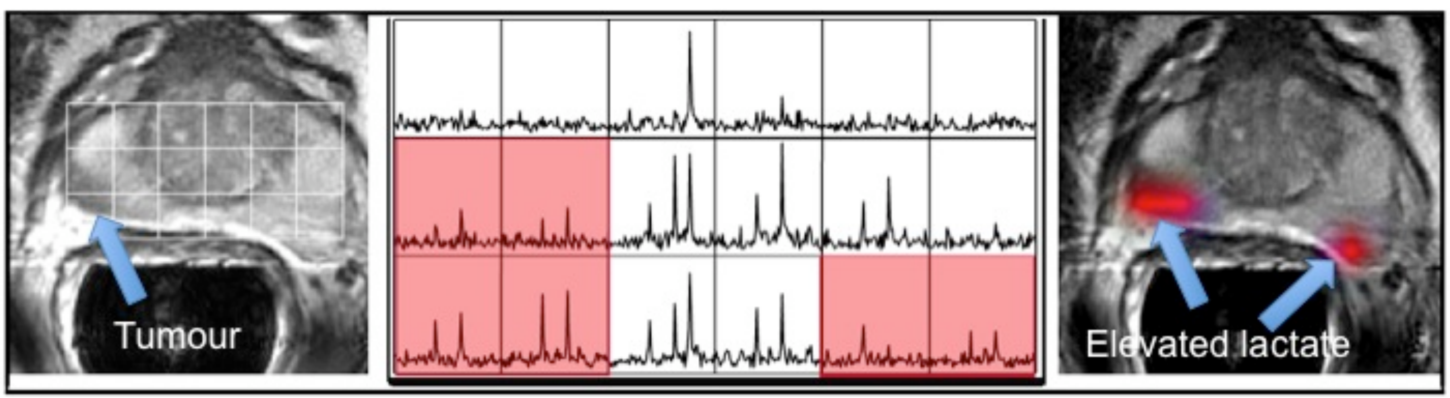




Gallagher FA, *et al* 2009, *PNAS* 106(47):19801

First human study using hyperpolorized C-13 pyruvate in prostate cancer



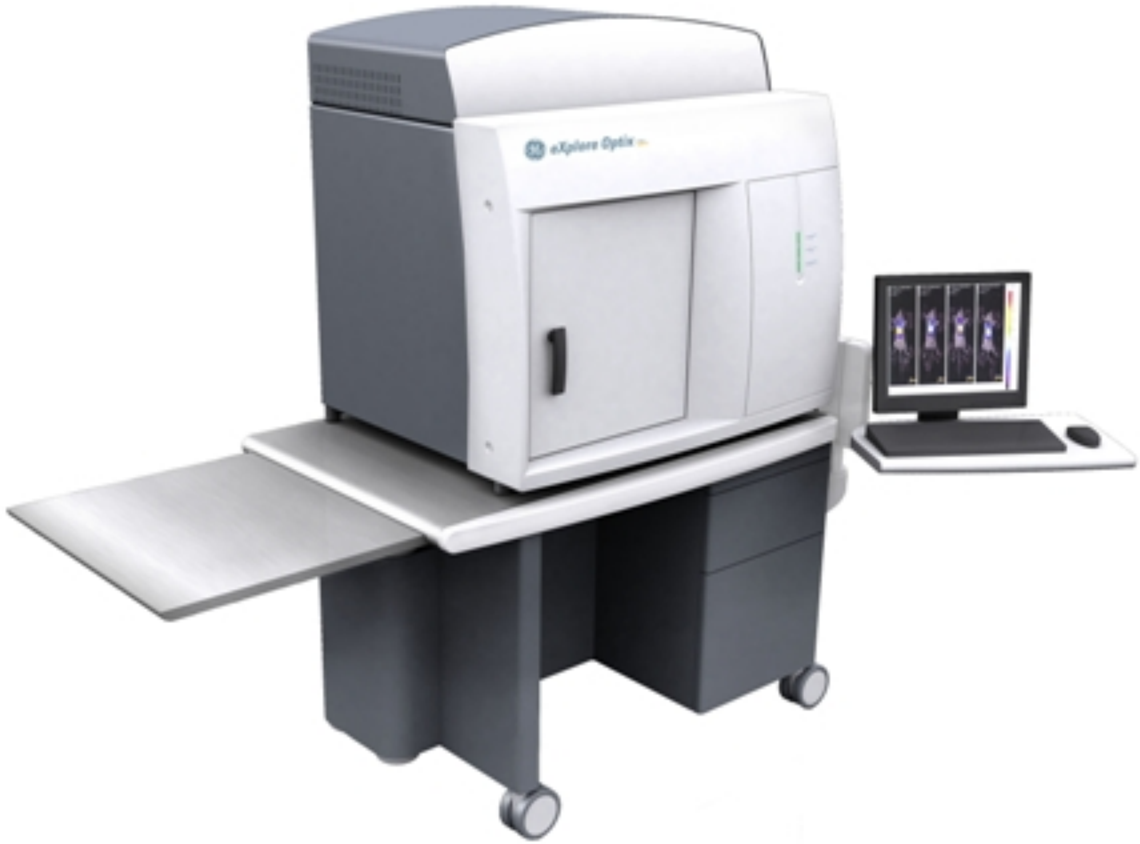


Nelson S *et al.*
Sci Trans Med 2013

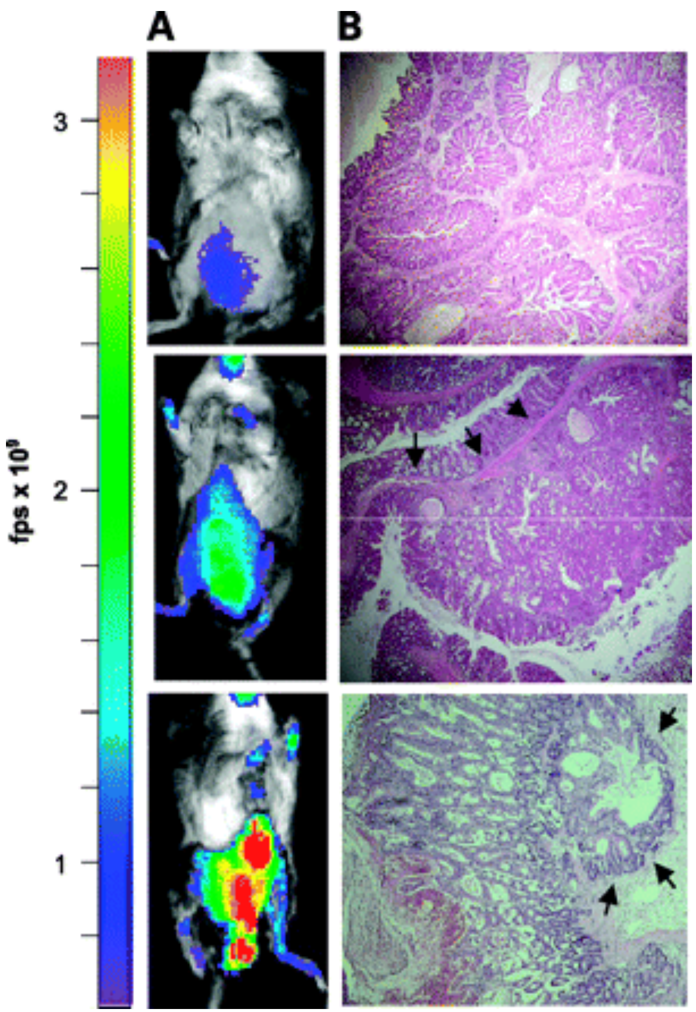
Optical imaging

- Uses visible light or near infrared
- Very high resolution
- Can be amplified using bioluminescence
- However problems of attenuation
- Explored mainly in small animals and surface tissues such as skin or GIT

Optical imaging device (note the object has to be inside the detector)



Optical imaging in Ca colon

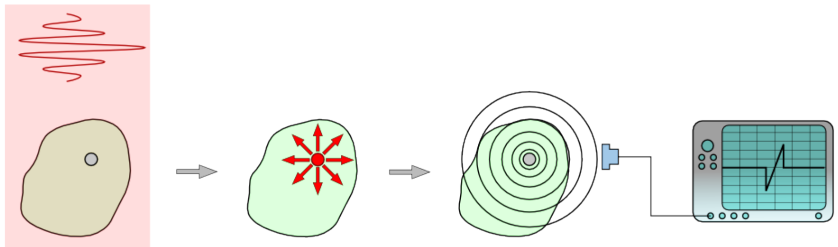


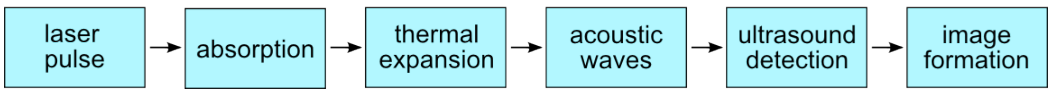
NIR-con-PK11195 is retained proportionately to tumor stage. **A.** Representative optical imaging of Smad3$^{+/-}$ (*top row*) and Smad3$^{-/-}$ (*middle and bottom row*) mice (fluorescence intensity indicated by photon flux per second). **B.** Matching H&E stains demonstrating hamartoma (*top row*; magnification, 100×), adenoma (*middle row*; magnification, 100×; *arrows,* uninterrupted muscularis mucosa), and carcinoma (*bottom row*; magnification, 50×; *arrows,* invasive component)

Photoacoustic imaging

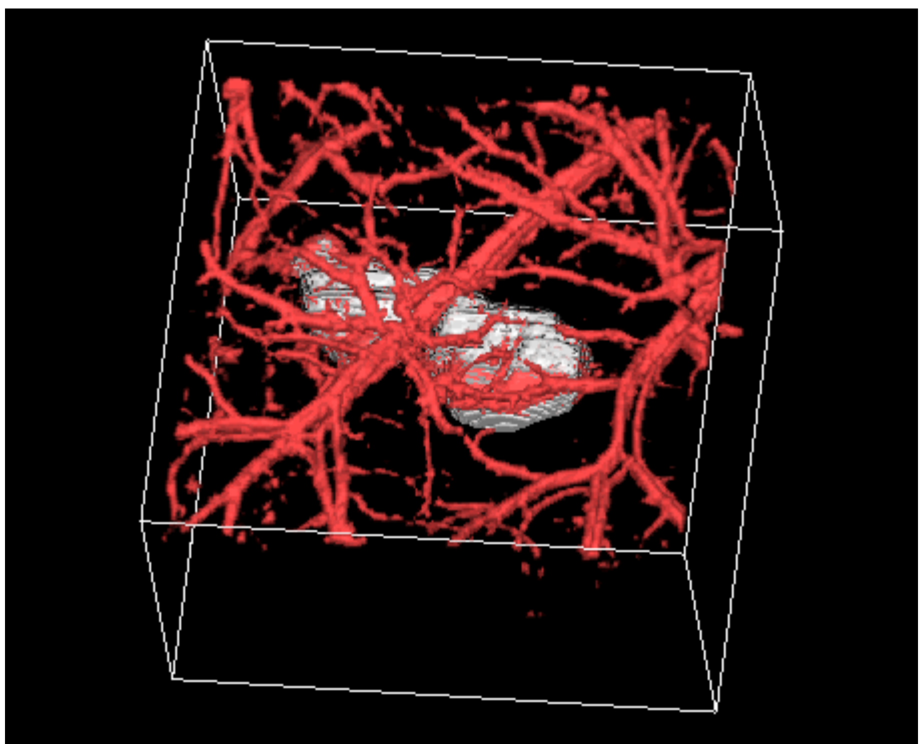
- Hybrid imaging
- Uses high frequency laser which can be tuned to a particular molecule
- Vibrates target tissue which heats
- As it cools releases ultrasound
- Can penetrate deeper into tissue than optical imaging

Photoacoustic imaging





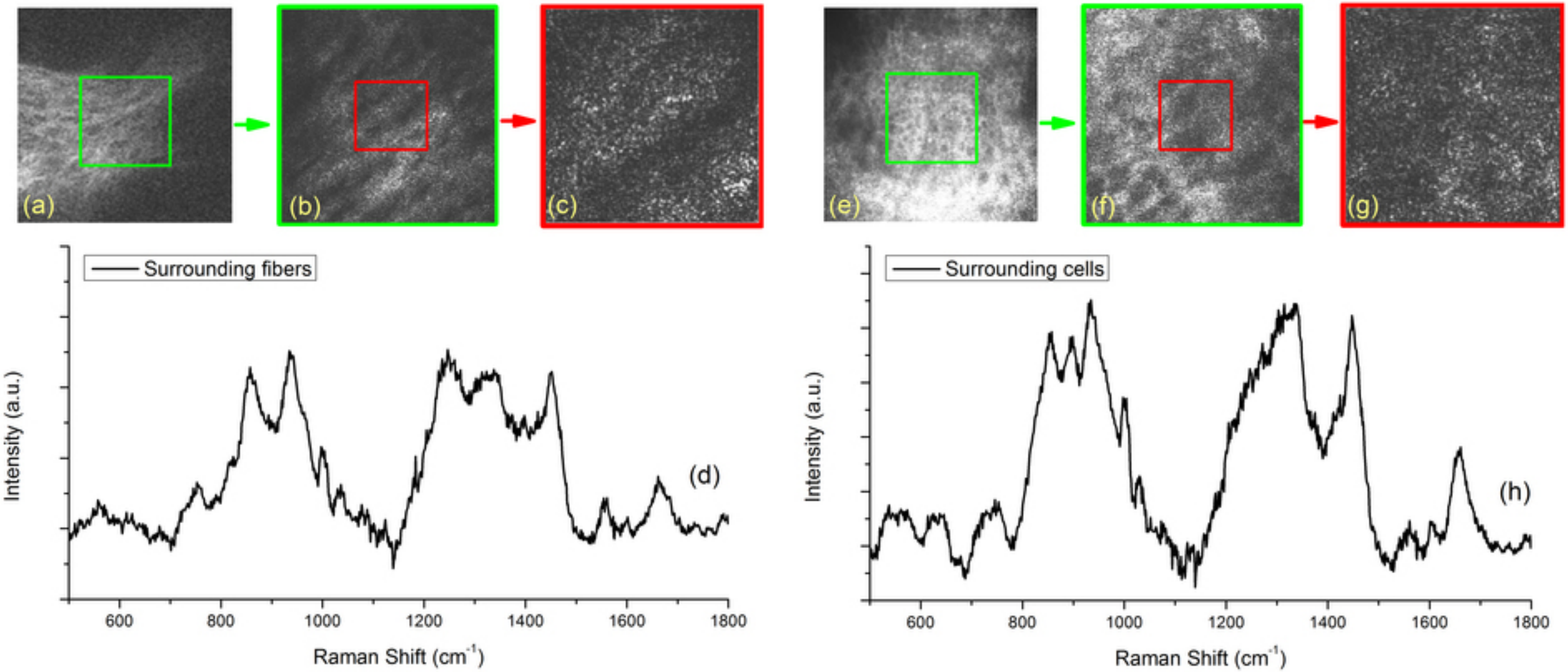
Red is blood, white is melanin containing cells



Ramen imaging

- Relies on the scattering of laser light through a substance
- Scattering depends on the inelasticity of tissue
- In cancer the increased perfusion of the tumour increases water content so less elastic
- Ramen imaging has very high resolution but minimal tissue penetration (best used with tissue biopsies)

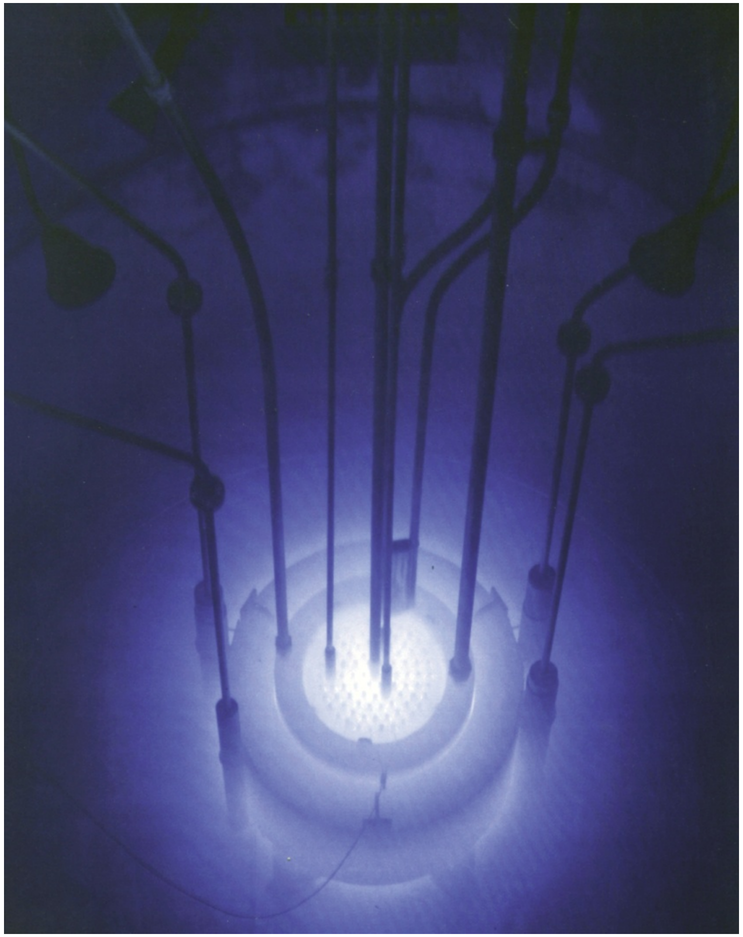
Wang et al Nature 2012



(a) SHG + TPF image of the fiber structures surrounding a blood vessel of the cherry angioma lesion, image FOV is 300 μm × 300 μm; (b) zoom-in *cw*RCM image of the area shown in the green square of (a), image FOV is 150 μm × 150 μm; (c) *cw*RCM image showing the ROI from the area of the red square in (b), the image FOV is 60 μm × 60 μm; (d) confocal Raman spectrum of the fiber structures of the red square area shown in (c) and (b), the exposure time is 20 s; (e) *fs*RCM image of the cellular structures surrounding a blood vessel of the cherry angioma lesion, image FOV is 300 μm × 300 μm; (f) zoom-in *cw*RCM image of the area shown in the green square of (e), image FOV is 150 μm × 150 μm; (g) *cw*RCM image showing the ROI from the area of the red square in (f), the image FOV is 60 μm × 60 μm; (h) confocal Raman spectrum of the cellular structures of the area shown in (f) and (g), the exposure time is 20 s.

What is this

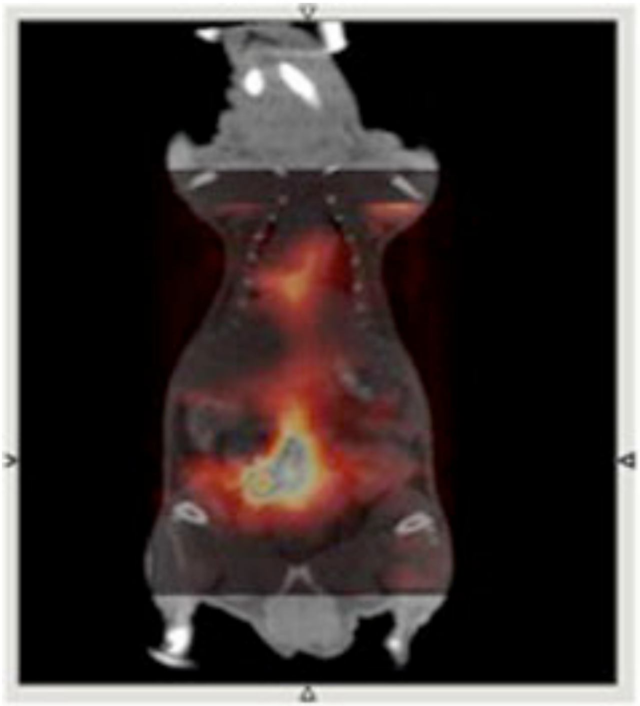
What is this



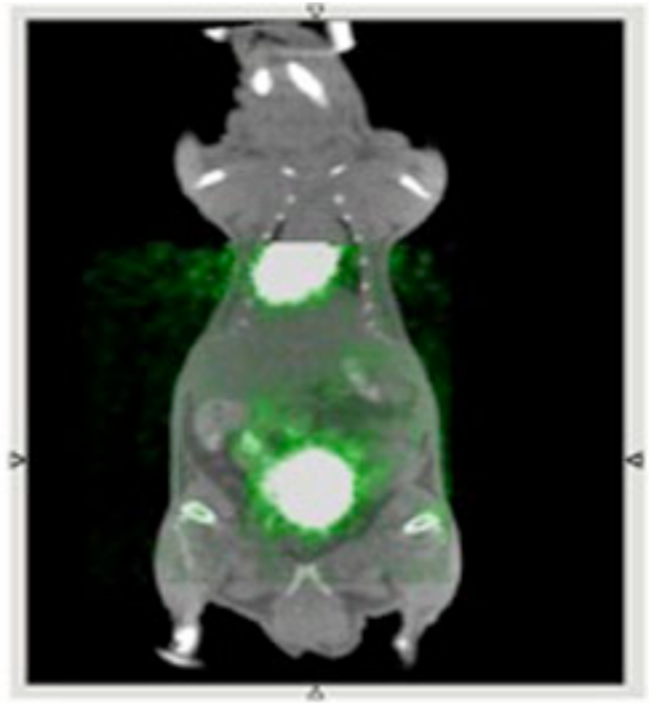
Cerenkov radiation

- When a sub-atomic particle travels faster than the speed of light it energises the structures it passes through
- The electrons shift to a higher orbit and as they return to normal emit a blue light
- Strangely enough the positron from F-18 does just that
- Back where we started?

Image from UC Davis



CT and CLT



CT and PET

Conclusion

- PET/MR will come but at US$4-5million will it ever be common
- Evidence base still shaky
- Problem with body coils
- Of the other imaging most likely to succeed is photoacoustic