



What's new, pussycat? (and tiger)



**Steve
Allen**

**11th September
2025**

**A personal
glimpse at the
present and
the future of
prostate
cancer**





*What is the
cheapest
treatment for
advanced
prostate
cancer?*

*What is the cheapest treatment for
advanced prostate cancer?*

Don't let it get to an advanced stage

What is the cheapest treatment for advanced prostate cancer?

Don't let it get to an advanced stage

Diagnose the cancer early whilst it is still localised

Utilise better imaging / diagnostics

Increased use of localised therapies

Use of earlier combined therapies



So much that
could be
discussed!!

Not enough time
to cover
everything



**Not all
treatments
discussed will be
suitable for
everyone**

**Not every PCa
unit will have
access to all
treatments**



**I know I am bad
at keeping to time**

**Shut me up when
you've had
enough!!!**



*What are the alternatives to
radical surgery?*



*Should we talk more about
local therapies?*



*Are we using a
sledgehammer to
crack a nut?*

Local Therapy

What types are there?

All focal therapies aim to destroy cancer cells locally without damaging surrounding tissues

- **Heat** HIFU High Intensity Focussed Ultrasound
- **Cold** Cryotherapy needles
- **Electricity** I.R.E High voltage electric pulses *Nanoknife*®
- **Poison** 'Local chemotherapy'
- **Frying** Focussed radiotherapy

Local Therapy

Is this a good option? Who can have it?

Newly diagnosed patients

- with low to medium risk cancers
- localised within prostate – no localised spread
- ? small tumour size

Local Therapy

What are the advantages?

Potentially less side effects

- Incontinence and sexual dysfunction

Often performed as day surgery

Catheter needed for shorter time

- Typically 3 days

Can normally be repeated if small recurrences occur

Local Therapy

What are the disadvantages?

Recurrence of cancer:

- 20% need 2nd focal therapy by 5 years
- 7% need radical treatment by 5 years

Requires different skills and expertise

- Very 'technology heavy' in equipment practical skill

Not yet widely available

- NHS / NICE guidance varied

? Inertia for change from conventional surgeons





*Can
radiotherapy
be made less
harmful?*

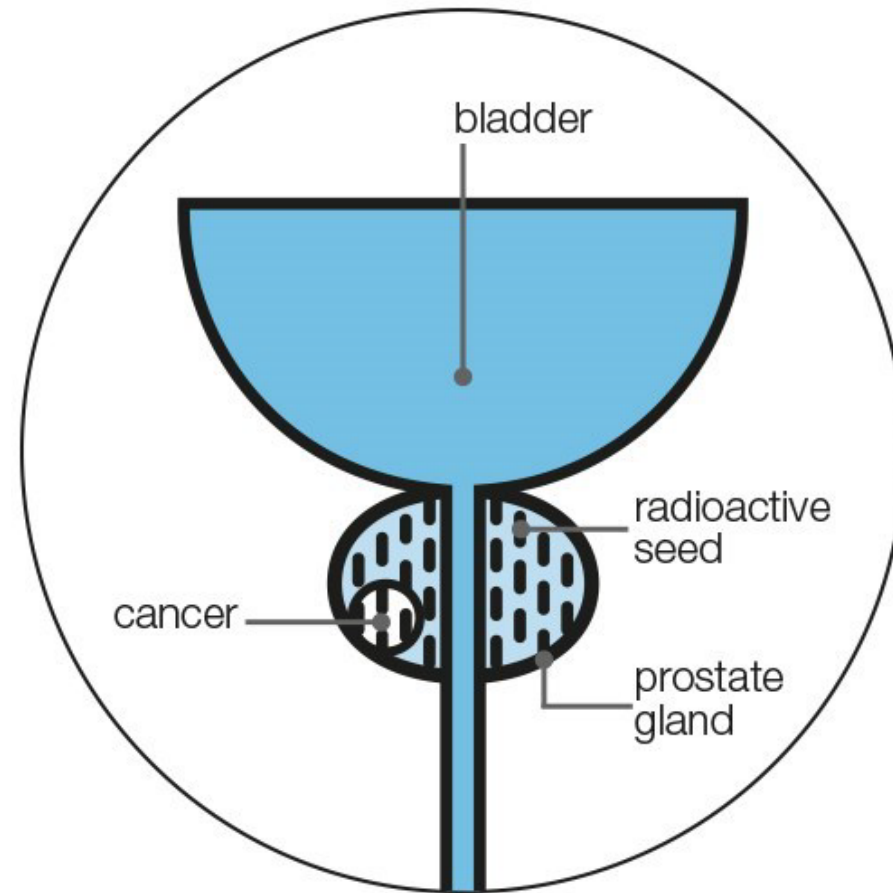
Local Therapy

Brachytherapy

Low-dose

Permanently implanted
seeds

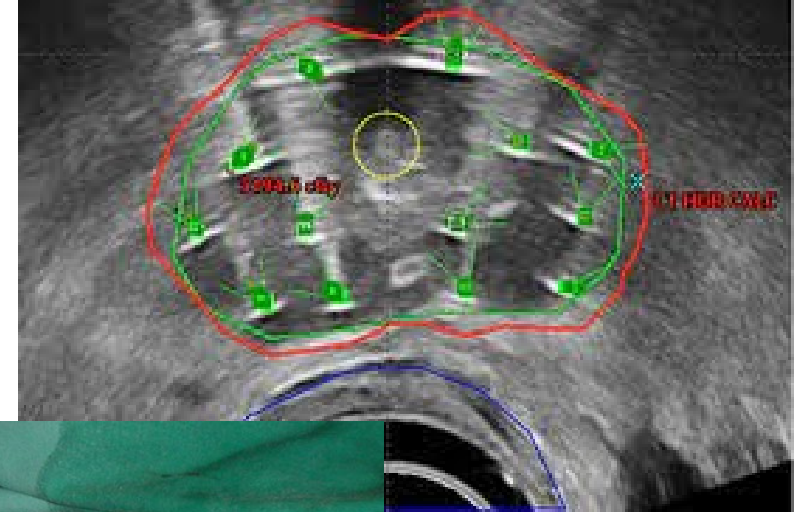
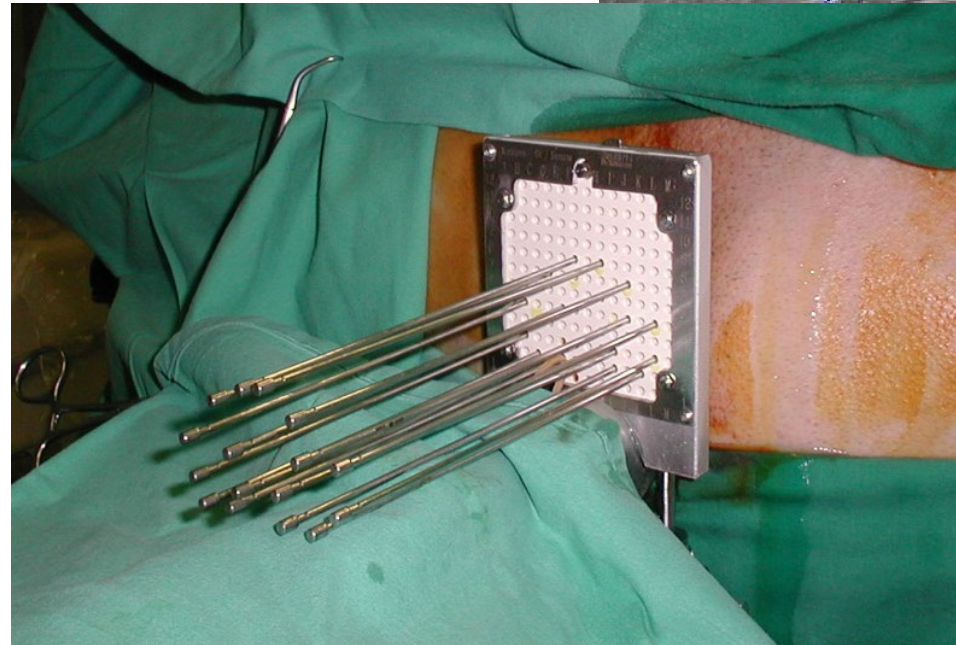
Acceptable S/E profile



Local Therapy

Brachytherapy

High dose /
brachytherapy boost



Local Therapy

Making external beam
radiotherapy less 'harmful'

Original standard
treatment regimes use
IMRT



Local Therapy

Intensity Modulated RadioTherapy IMRT

Average 35 sessions

Uses 3D planning images to customise the treatment plan

Shape and intensity of the radiation beam varied after each movement of the treatment head around the body



Local Therapy

Image Guided Intensity Modulated RadioTherapy

IGIMRT IGRT

Use of more focussed and more powerful beams

‘Hypofractionation’ - 20 sessions

Employs CT imaging during treatment to verify the position of the tumour and the patient.

Allows for real-time adjustments to the radiation



Local Therapy

Stereotactic Ablative Radiotherapy (SABR)

Ultra-hypofractionation
(5 - 7 sessions)

Localised treatment of single metastases

Current IGRT machines may be able to be adapted to do this therapy



SABR

Uses multiple narrow beams from many different angles

Requires accurate localisation of prostate at each session

May require the insertion of metallic markers visible on CT

Gold fiducials



Cyberknife®

Cyberknife® is a more advanced form of SABR but requires a dedicated machine

Continuous monitoring using fiducials needed and dosage alteration possible



Cyberknife®

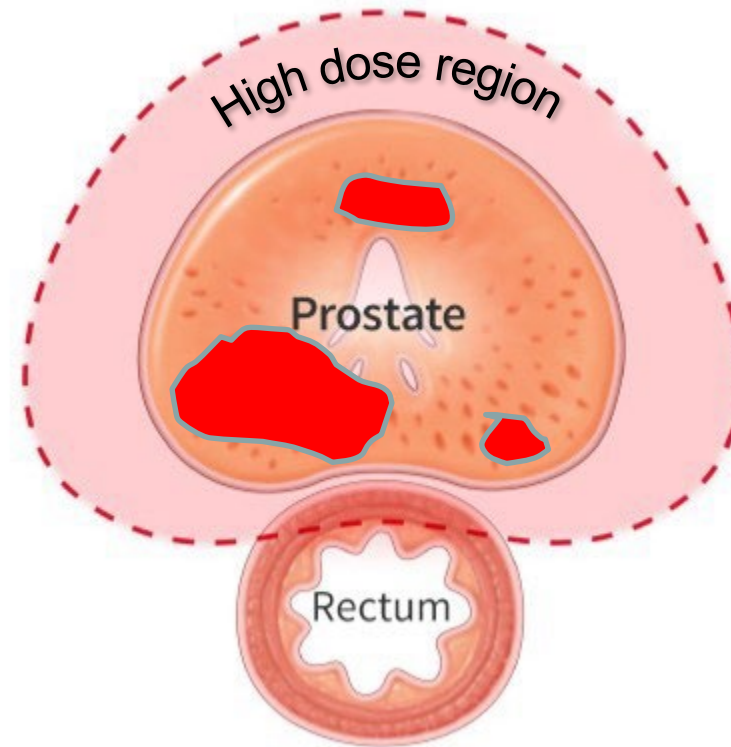
Use of rectal spacers

External beam RadioTx

Need to minimise
collateral damage to
rectum

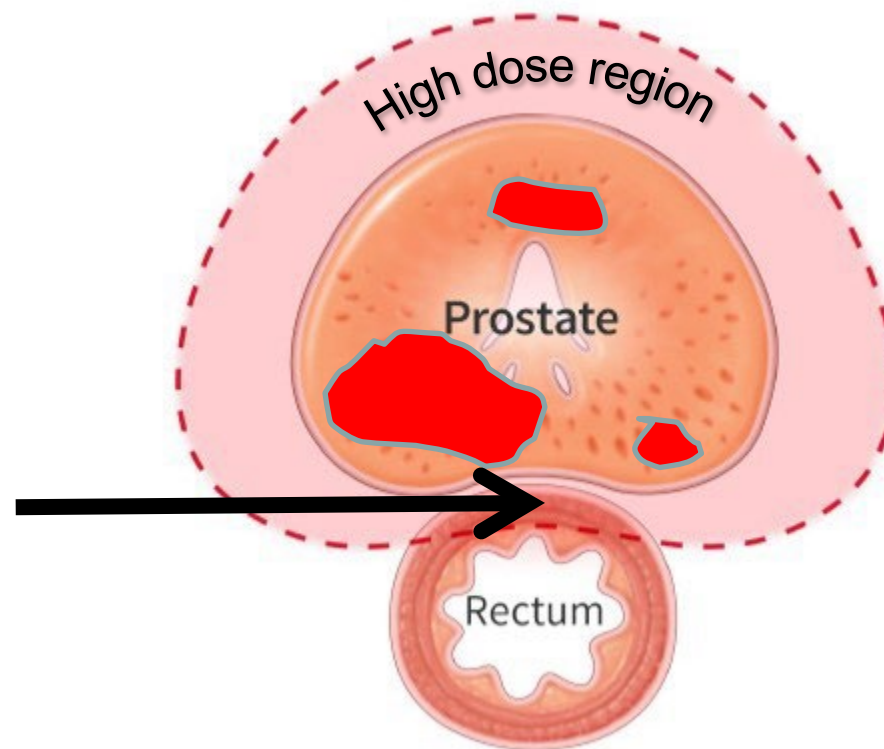
Essential if tumour is
peripheral and
posterior

- High dose field
extends beyond the
prostate capsule



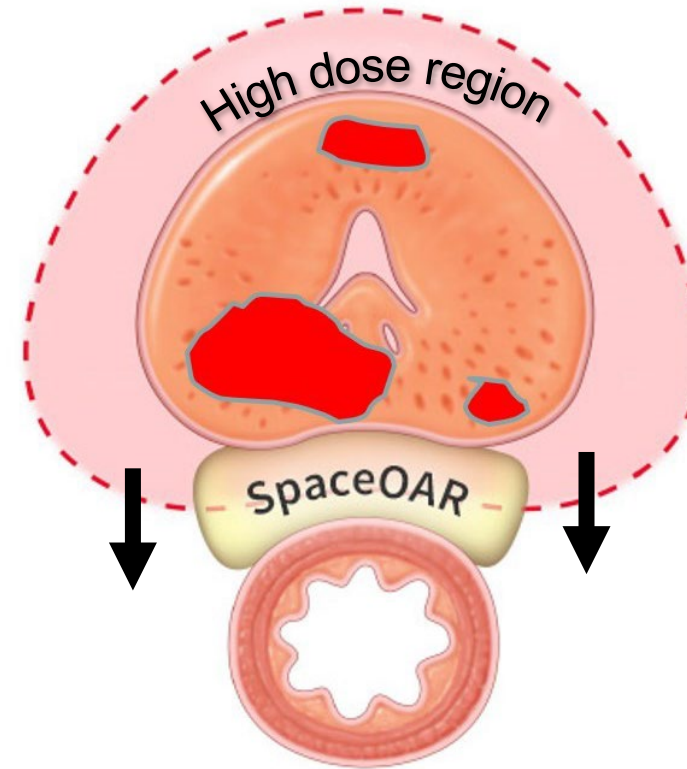
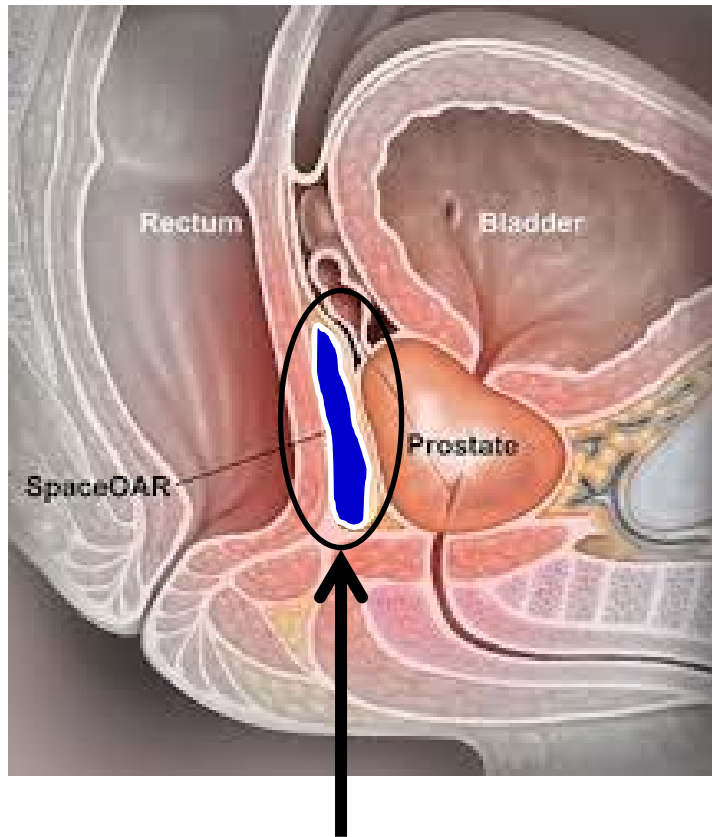
External beam RadioTx

- The answer is simple:
- Increase space between prostate and rectum

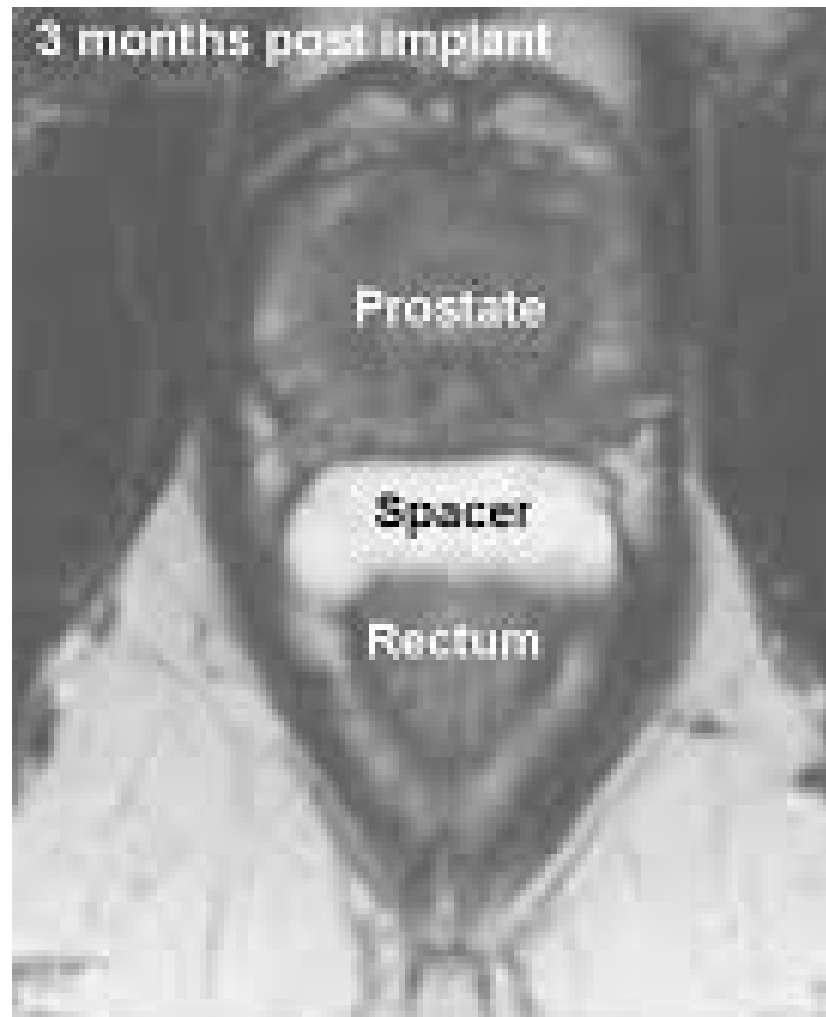


SpaceOAR®

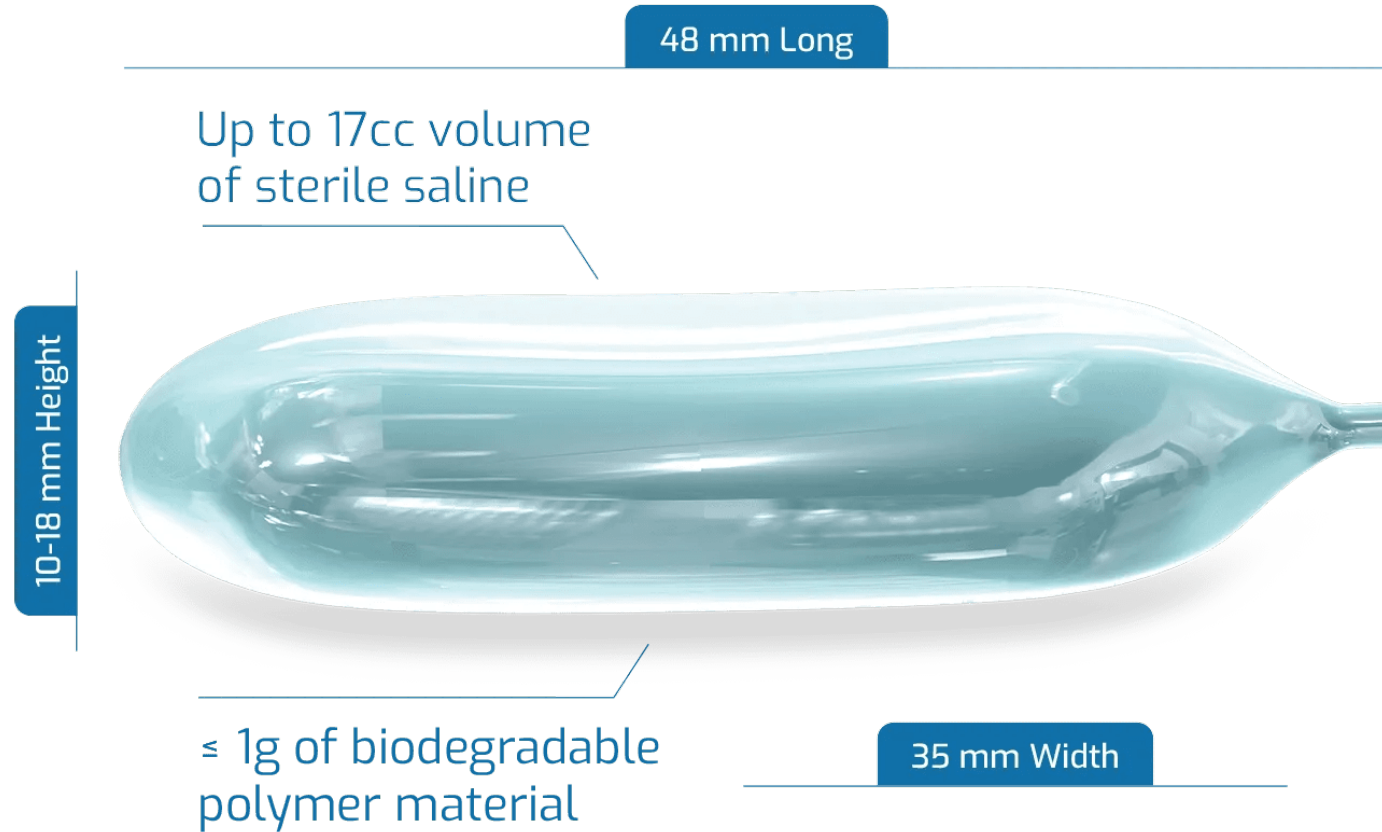
Injectable gel



SpaceOAR®



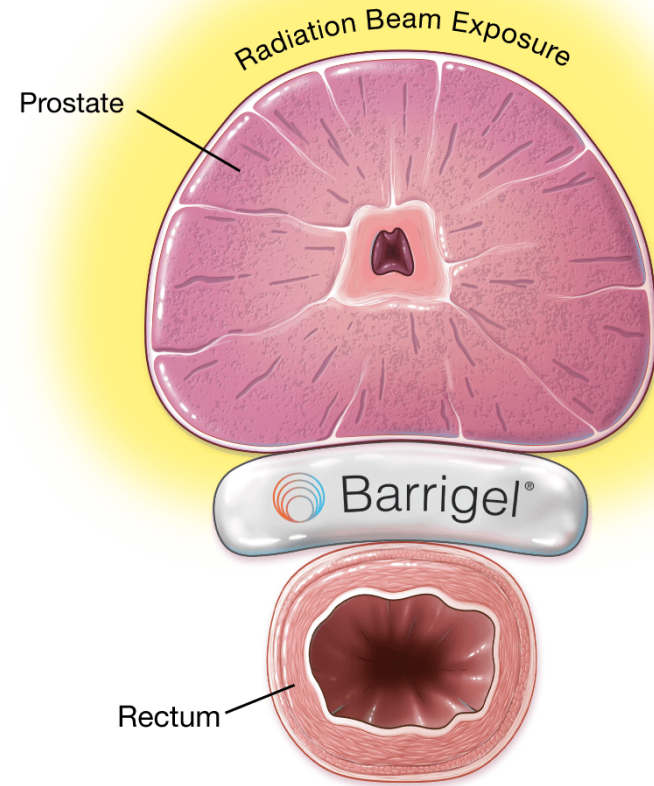
Other rectal spacers



Bio-Protect[®]
Inflatable
bio-degradable balloon

Other rectal spacers

Barrigel®
Hyaluronic acid gel



Raypilot®

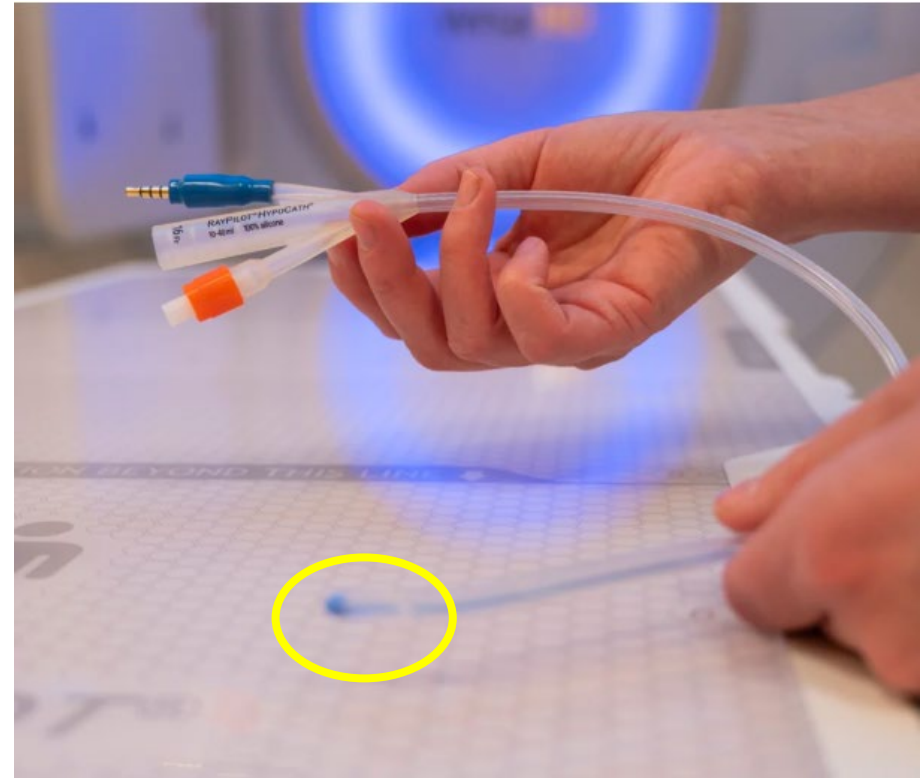
A system which continuously monitors position and motion of prostate/bladder using a urinary catheter with transmitter and a special mattress/receiver.



Raypilot®

A specialised catheter contains a device which continually emits a radio wave

-



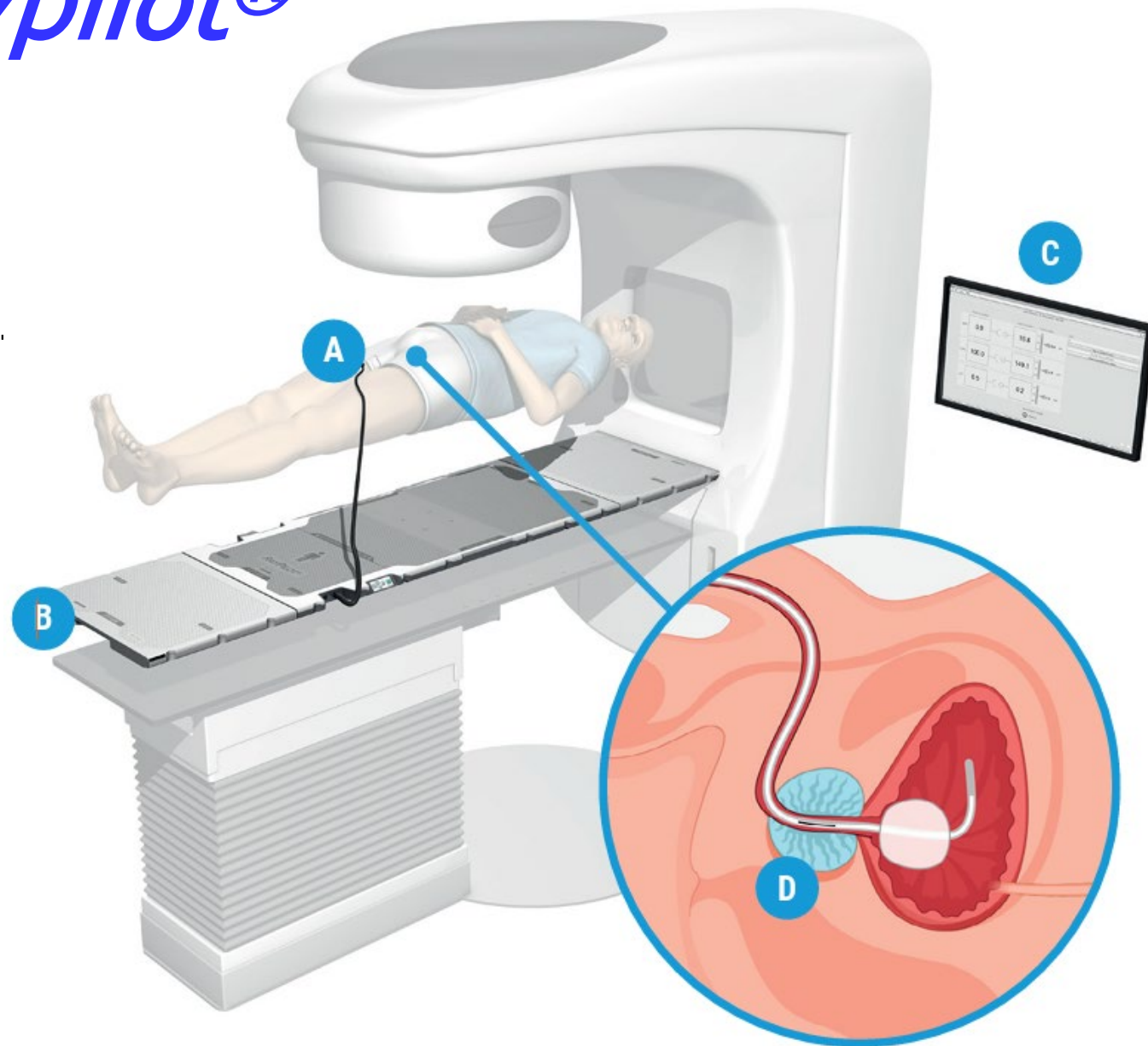
Raypilot®

The patient lies on a unique mattress which contains an array of sensors to pick up the radio signals and monitor the position of the bladder and prostate



Raypilot®

The dedicated software then monitor and adapt radiotherapy intensity in response to patient movement



Advantages of all these developments

Highly localized radiotherapy beams

Reduction in damage to rectum / bowel

Enables larger doses therefore less visits

Less visits better for patient but also frees up equipment for other patients



Which system is best???



Not my
problem!!



*What's new in
drug therapy?*



Treatment of newly
diagnosed
metastatic hormone
sensitive PCa



Initial therapy

Use hormone therapy
(ADT) as single therapy



Double / twin therapy

Use 2 drugs together

ADT + chemotherapy
(docetaxel)

Introduced as a result of part of Stampede Trial

- Obvious improvement in outcome led to early adoption as standard treatment



Then came Covid!.....

Concern about
immunosuppression
produced by chemo

part of Stampede
improvement in outcome led
early adoption as standard
treatment



Double / twin therapy

Use 2 drugs together

Keep ADT

Replace chemo with

- Abiraterone
- Enzalutamide

Rapid assessment and approval by NICE
and SMC

- NICE – Enzalutamide
- SMC – Abiraterone (and now Enza)



But now things have
progressed even
further.....

Triplet therapy

Use 3 drugs together



Triplet therapy

ADT

+

Chemotherapy

+

NHA / ARTA / ARPI



Enzalutamide

Abiraterone

Darolutamide

Apalutamide

Triplet therapy

ADT

+

Chemotherapy

+

NHA / ARTA / ARPI



Enzalutamide

Abiraterone

Darolutamide

Apalutamide

Triplet therapy

ADT

+

Chemotherapy

+

NHA / ARTA / ARPI



Darolutamide

Already approved for treatment of
non-metastatic hormone resistant PCa
'Biochemical recurrence'
*Rising PSA but no mets on conventional
scanning*

Triplet therapy

ADT

+

Docetaxel

+

Darolutamide



Additional side effects from addition of Darolutamide are very low

Main S/E from Docetaxel chemotherapy

Approved by NICE & SMC 2023



*What about
PCa that's
already
hormone
resistant and
metastatic??*

Metastatic hormone resistant PCa

Patient already on Hormone therapy but now has metastases

- May have already had other radical Rx
 - Surgery Radical radiotherapy

Conventional treatment is to add NHA / ARTA

- Abiraterone Enzalutamide

Twin or Dual therapy now standard in this situation



Metastatic hormone resistant PCa

Time for TRIPLET therapy
to be added

ADT

+

Abiraterone

+

???????



Metastatic hormone resistant PCa

Time for TRIPLET therapy
to be added

ADT

+

Abiraterone

+

Olaparib



Shown to improve outcomes over adding
Abiraterone & ADT

Approved by NICE Feb 2024

Metastatic hormone resistant PCa

Time for TRIPLET therapy
to be added

ADT

+

Abiraterone

+

Olaparib

NO requirement
to know BRCA
genetic status

17% men with
advanced PCa
have BRCA
abnormality



Shown to improve outcomes over adding
Abiraterone alone

Approved by NICE Feb 2024



"I've got to go on hormone treatment but I don't fancy those painful injections."



*"Surely there
must be a
tablet I can
take?"*

Current drugs used are all given by depot injection

LHRH analogues:

Goserelin **Zoladex**[®]

Leuprorelin acetate **Prostap**[®] or Lutrate[®]

Triptorelin Decapeptyl[®] or Gonapeptyl Depot[®]

Buserelin acetate Suprefact[®]

*All produce an initial rise in testosterone / PSA
and the negative effects of this on PCa prevented by
co-prescribing of Bicalutamde*

Current drugs used are all given by depot injection

LHRH antagonists:

Degarelix Firmagon®

This does not produce an initial surge of testosterone.
It is often used where there are bone metastases near the spine at danger of producing spinal cord compression and immediate treatment is vital

So, what's the alternative?

LHRH antagonists

Relugolix Orgovyx[®]

Given as oral dose once daily

Similar mode of action to Degarelix

Is it any good?

Relugolix Orgovyx®

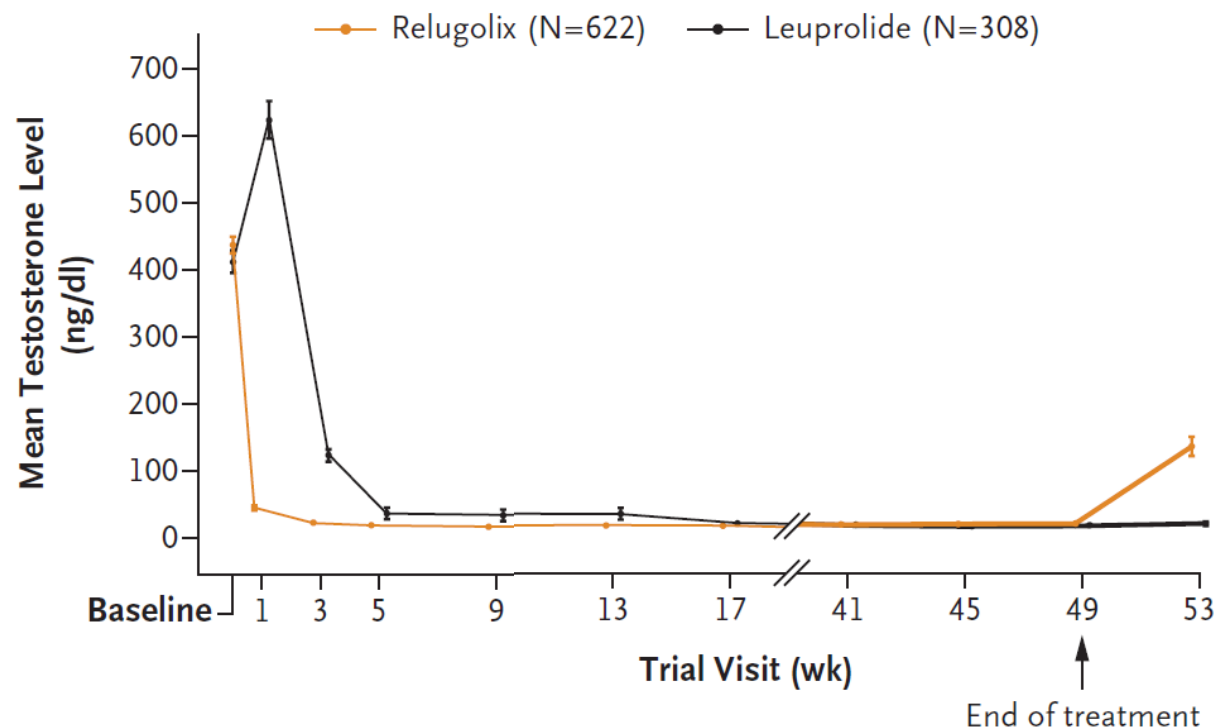
Compared to injectable LHRH agonist
(HERO trial)

Equal or superior reduction in
testosterone

Faster onset of testosterone
reduction

No testosterone 'surge'

B Mean Testosterone Level among All Patients



Is it any good?

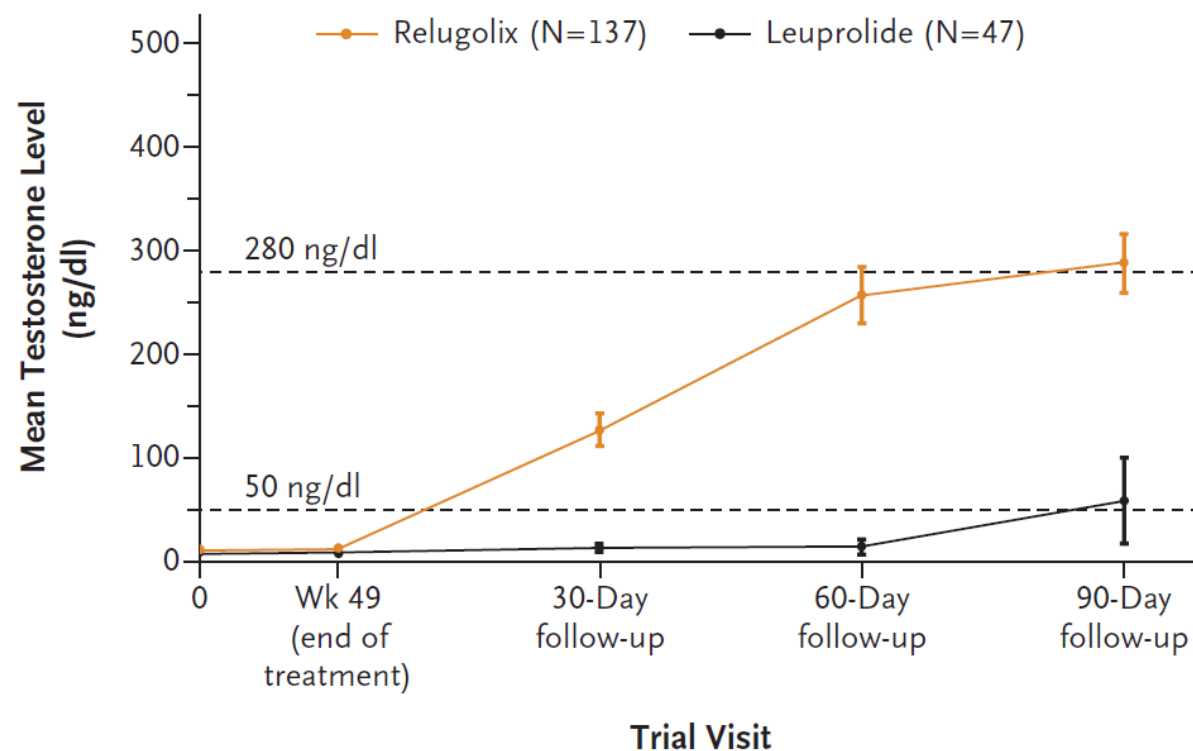
Relugolix Orgovyx®

Compared to injectable LHRH agonist
(HERO trial)

Faster recovery of
testosterone after stopping
treatment

? Of advantage in 'fixed term'
treatment

C Mean Testosterone Level in Subgroup Followed for Testosterone Recovery

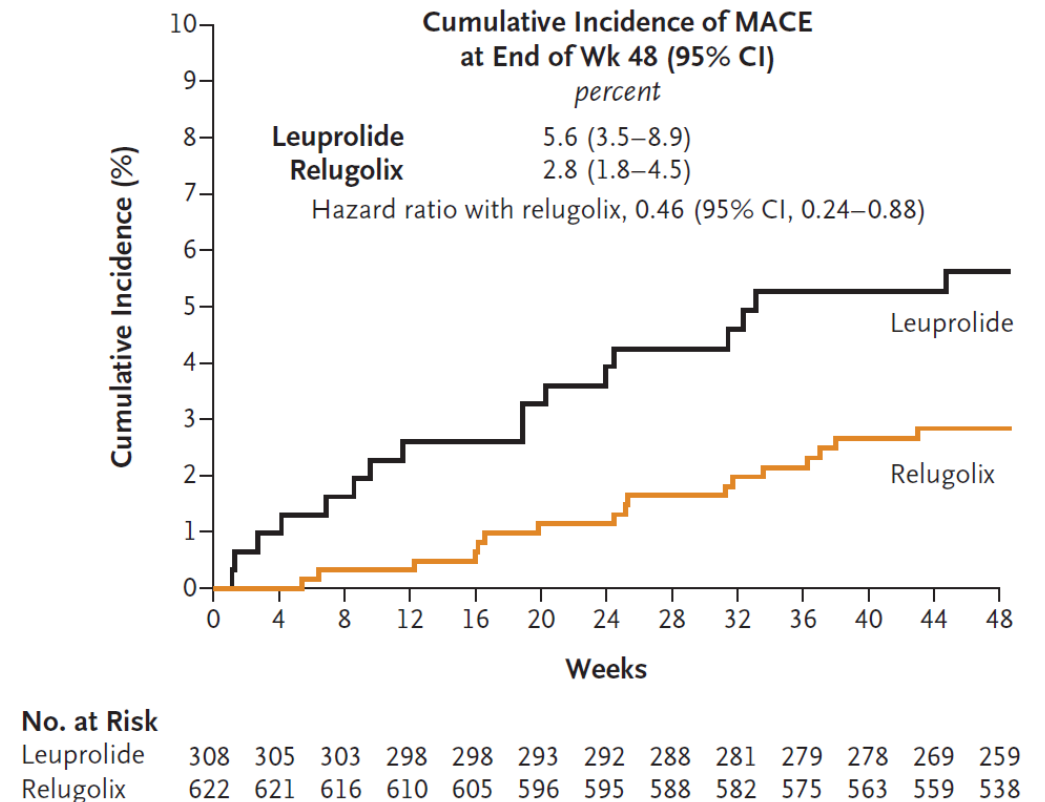


So, what's new?

Relugolix Orgavix®

Compared to injectable LHRH agonist
(HERO trial)

Overall incidence of S/E
equal or lower





BUT WAIT..

EVEN

THERE'S MORE..



*"What are all
these new
scans? Is one
better than
another?"*

A brief history of 'normal' imaging

- Conventional Imaging:
 - Plain X-rays
 - Roentgen **1896**



Josef Albert, München, repr.

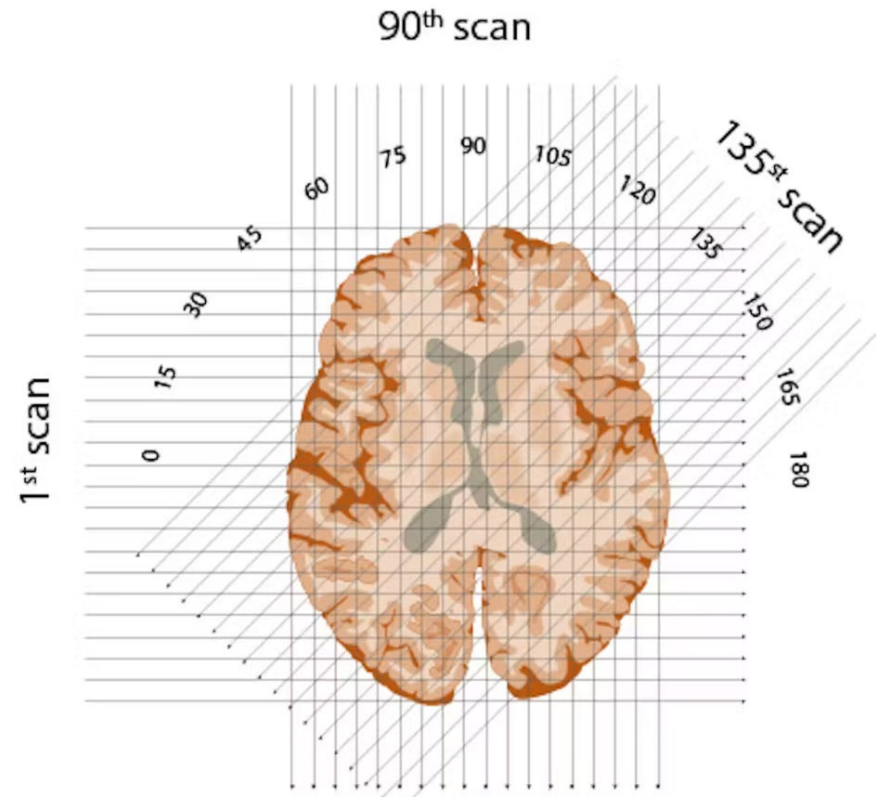
Hand des Anatomen Geheimrath von Kölliker.
Im Physikal. Institut der Universität Würzburg
mit X-Strahlen aufgenommen
von **Professor Dr. W. C. Röntgen.**

A brief history of 'normal' imaging

CT Scanning

Uses X rays to 'slice' up the body

Introduced by EMI engineer Godfrey
Hounsfield Radar engineer in WW 2



A brief history of 'normal' imaging

First clinical CT in 1971

Brain scan

Took 30 mins to perform

2hrs 30 mins to process the
data stored on magnetic tape



A brief history of 'normal' imaging

First clinical CT in 1971

Brain scan

Took 30 mins to perform

2hrs 30 mins to process the data stored on magnetic tape



A brief history of 'normal' imaging

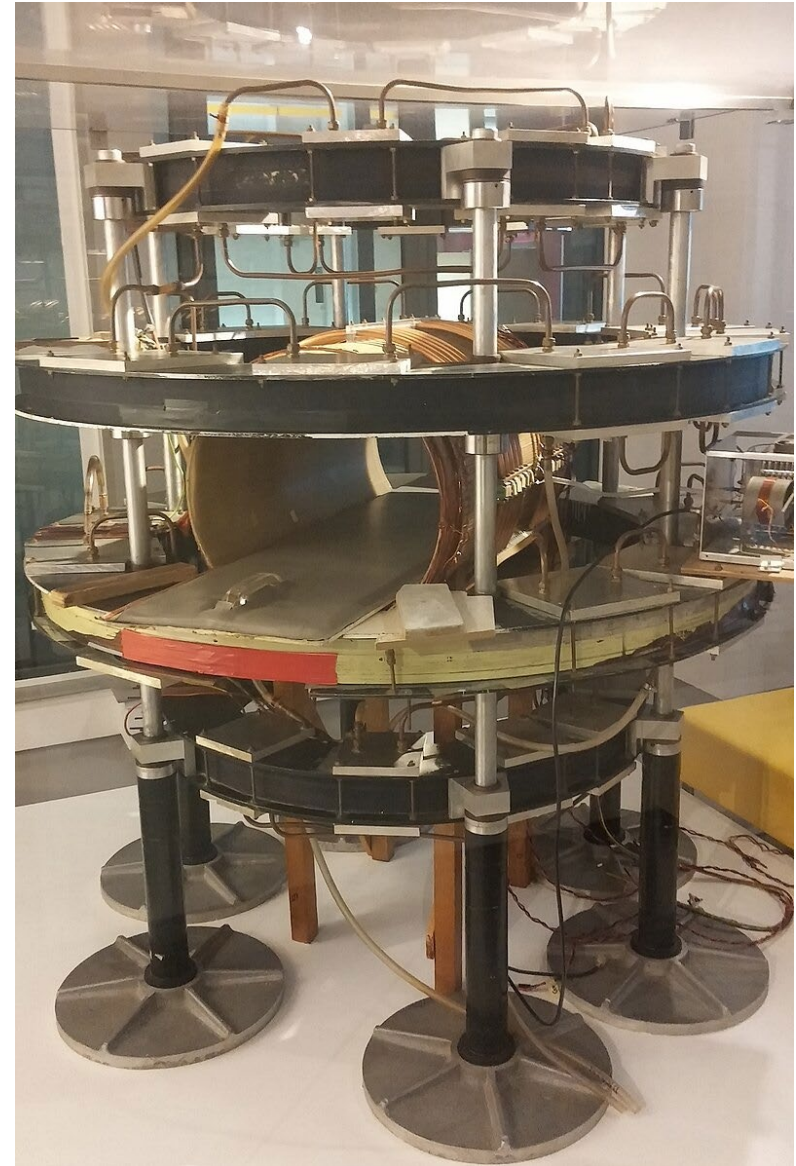
MRI scanning

Physical principal of NMR (Nuclear Magnetic Resonance) first described in 1944

Uses changing magnetic fields to produce radio waves from which images are constructed

Not developed into Magnetic Resonance Imaging until 1970's

1980 – first clinical use of a whole body MRI scanner in UK



Modern scanners
are a lot different!

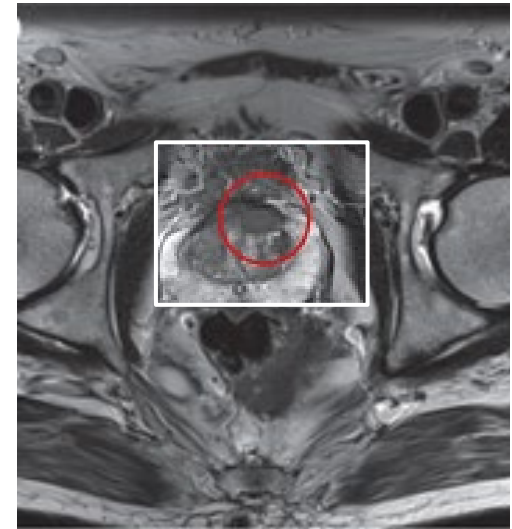
The stronger the
magnet, the better
the image quality.



A brief history of 'normal' imaging

Multiparametric MRI has changed everything in diagnosis of prostate cancer

Not evolved fully until early 1990's



PI-RADS

PI-RADS 1 = Very low (clinically significant cancer highly unlikely)

PI-RADS 2 = Low (clinically significant cancer unlikely)

PI-RADS 3 = Intermediate (clinically significant cancer equivocal)

PI-RADS 4 = High (clinically significant cancer likely)

PI-RADS 5 = Very high (clinically significant cancer highly likely)

**Prostate Imaging–Reporting
and Data System**

A brief history of 'normal' imaging

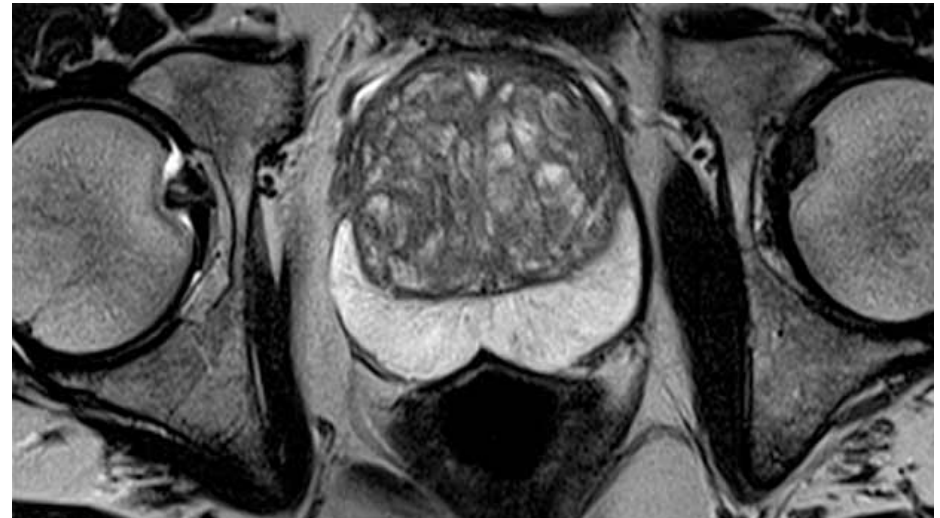
PROSTAGRAM

Simplified version of mpMRI

- Takes 10 - 15 minutes
- ? Better than PSA at finding aggressive PCa

Re-Imagine Trial
(UCL)

TRANSFORM
(Imperial/PCUK)



A brief history of 'normal' imaging

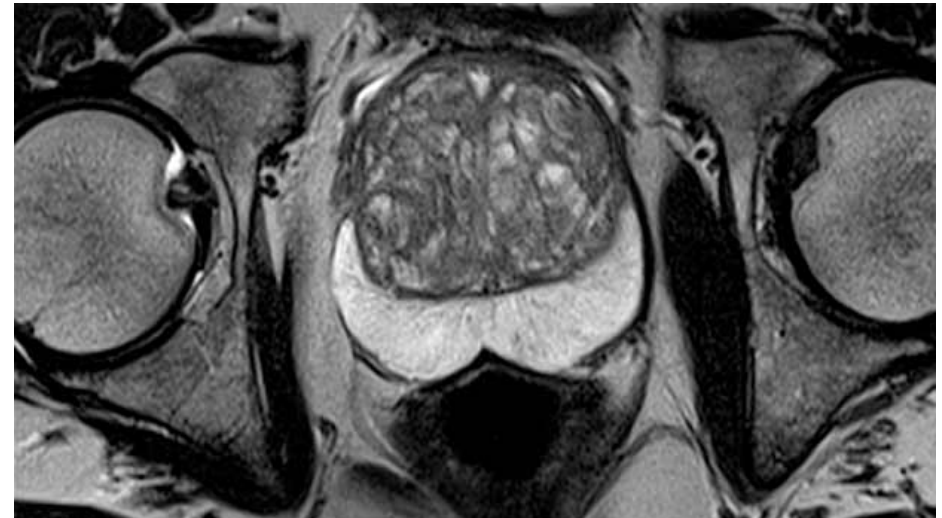
PROSTAGRAM

Simplified version of mpMRI

- Takes 10 - 15 minutes
- ? Better than PSA at finding aggressive PCa
- ? Avoid the need for a DRE?
- ? Use in place of PSA for screening certain groups?
 - Black men

Re-Imagine Trial
(UCL)

TRANSFORM
(Imperial/PCUK)



Improved imaging

WB-DWI

Whole body diffusion weighted MRI

- More accurate than bone scanning to assess the response of bone metastases to therapy
- Computer software to assist assessment
- May also identify lymph nodes



What about ultrasound?

Trans-rectal ultrasound has again developed over the years

1960's first shown but very poor quality

1974 first clinically useful scans
progressive improvements in quality

2023 Micro-US High resolution ultrasound

MRI fusion of U/S and MRI images

Use in transperineal Bx



'Normal' scans

MRI / CT – 'passive' scans

Demonstrates size, position and character of the tumour by looking at 'tissue density'

What is often needed is something to show *activity* of tissues

Particularly when investigation increasing PSA levels and onset of metastatic disease



*"So, tell me
about all these
new scans? Is
one better
than another?"*

What are the new scans?

PET scan

PSMA Scan

What is a PET scan?

PET - **P**ositron **E**mission **T**omography

PET – ‘active’ scan

Demonstrates cell activity

A low-dose radio-active molecule is introduced into the actual metabolism of the cell.

As the low dose radioactive tracer degrades, it gives off a ‘positron’

Positrons are ‘positive electrons’

Can be detected in a special scanner

What is a PET scan?

PET - **P**ositron **E**mission **T**omography

F¹⁸ FDG

Fluorodeoxyglucose

The more active the cell is,
the more positrons given off
and the the area shows up
on the scanned image



What is a PET scan?

PET - **P**ositron **E**mission **T**omography

Other tracers are now used in PCa:

C¹¹ choline

important in making cell walls

More sensitive for PCa cells

Not easy to manufacture

Occasional supply problems

F¹⁸ Fluciclovine

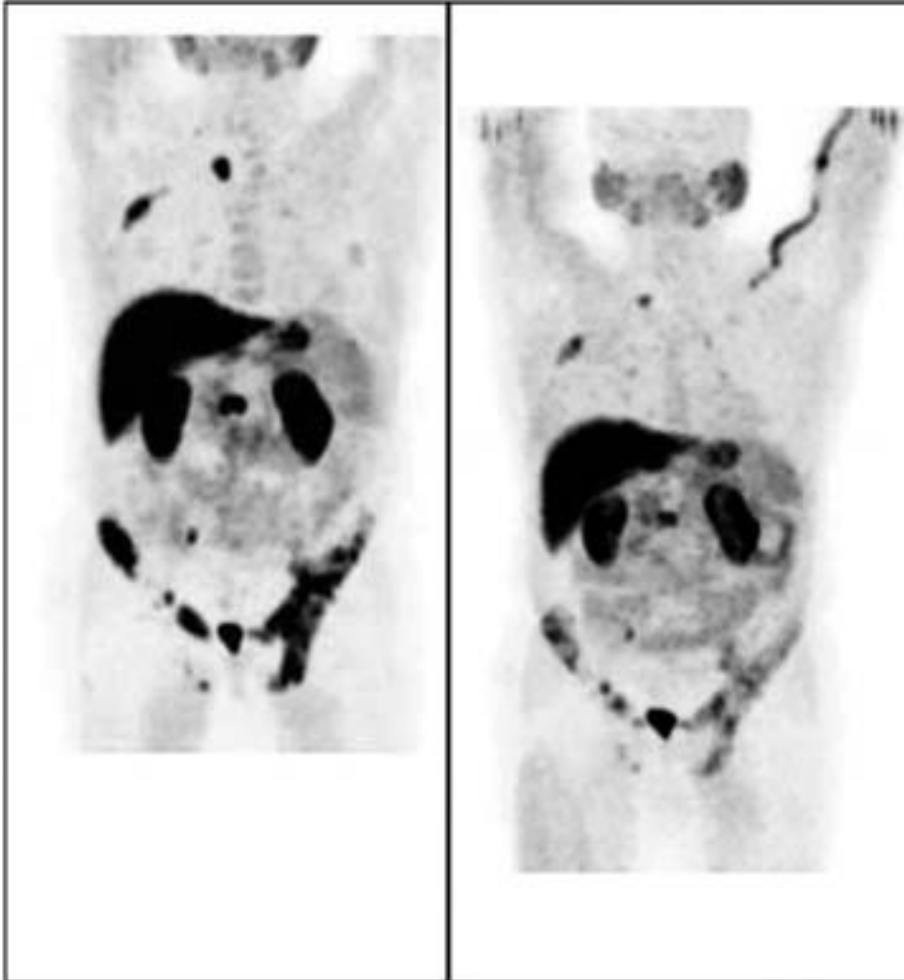
Choline PET scan

A. PSA: 149.0 ng/ml



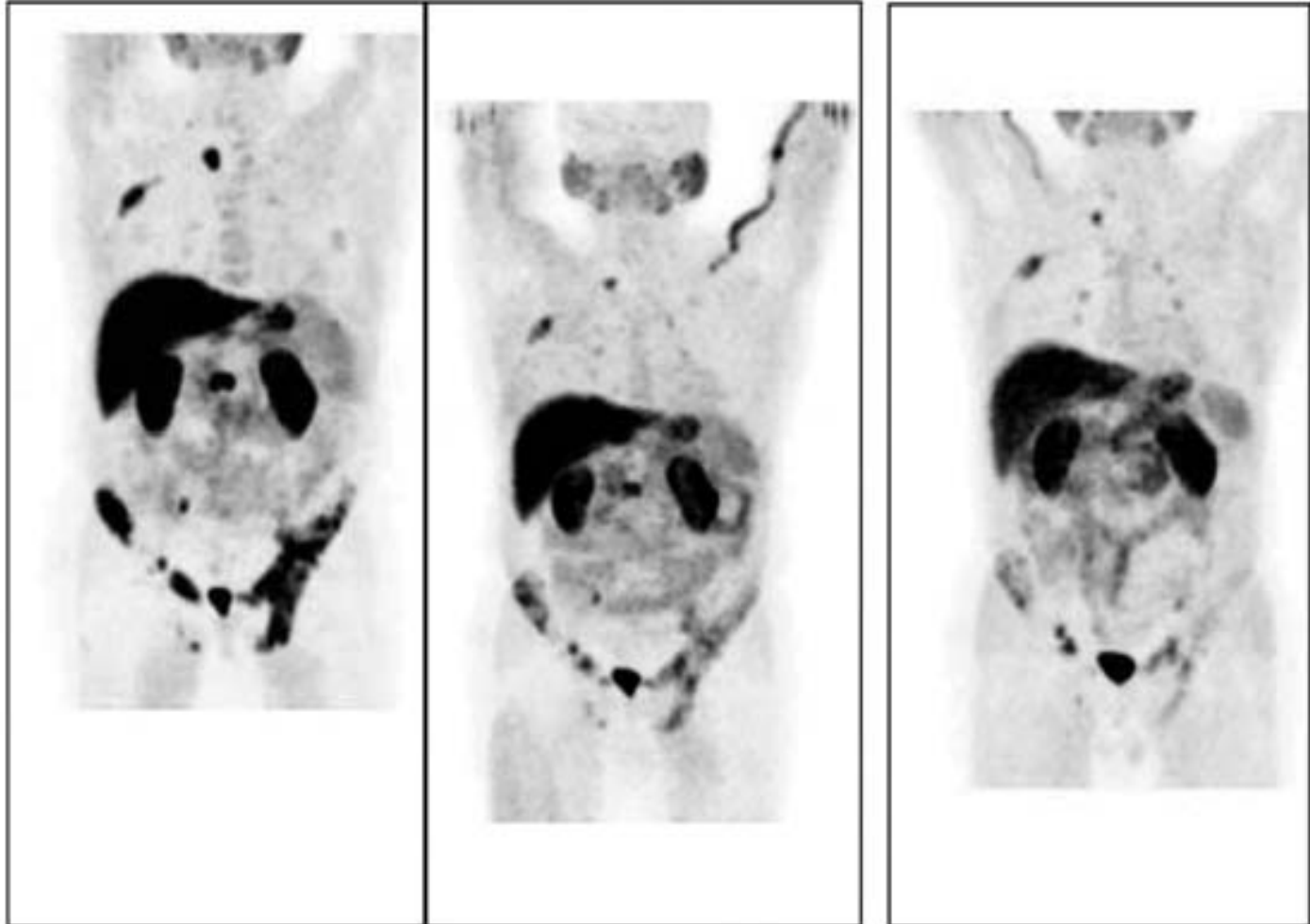
Choline PET scan

A. PSA: 149.0 ng/ml B. PSA: 44.99 ng/ml



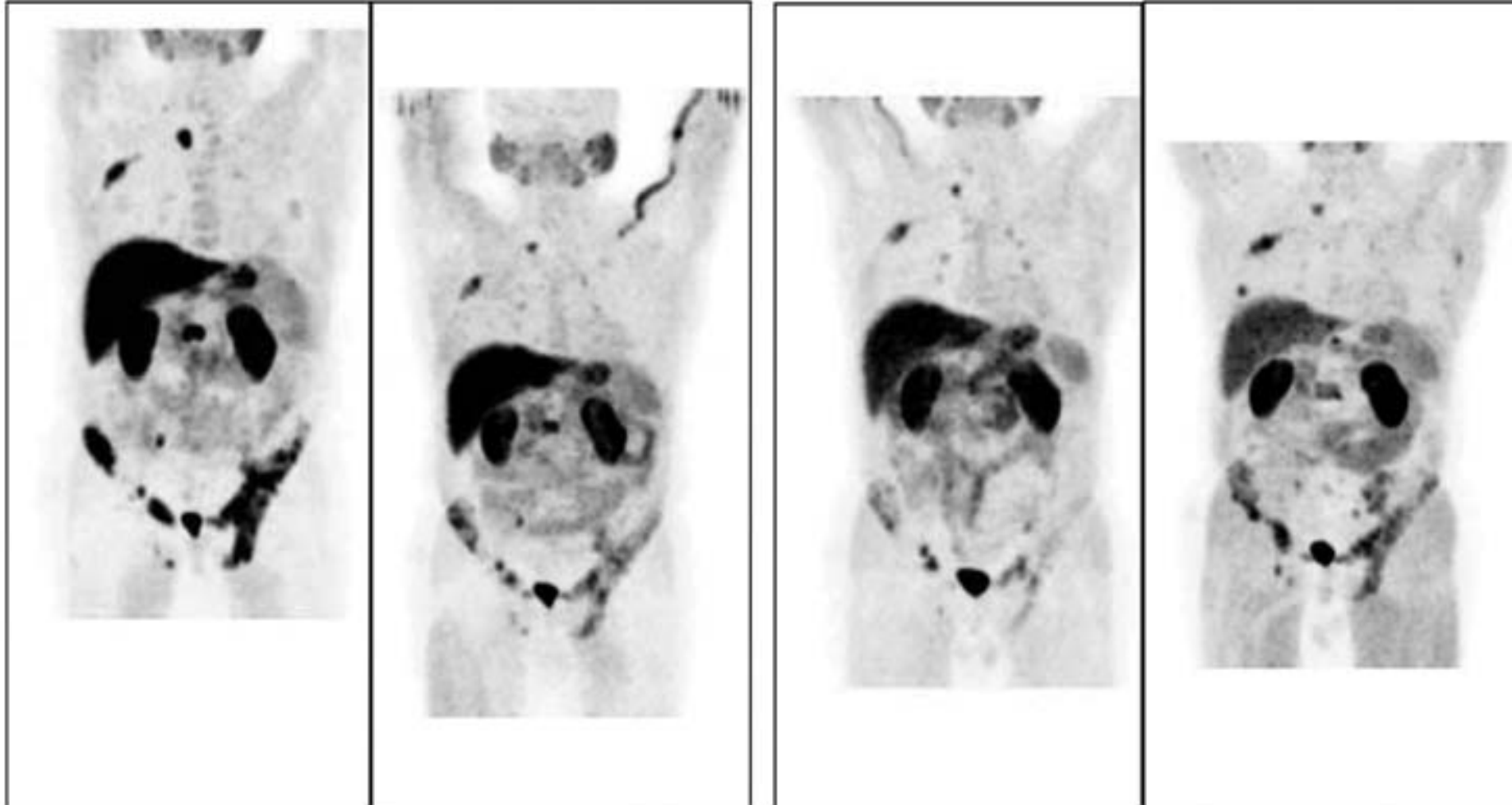
Choline PET scan

A. PSA: 149.0 ng/ml B. PSA: 44.99 ng/ml C. PSA: 40.0 ng/ml



Choline PET scan

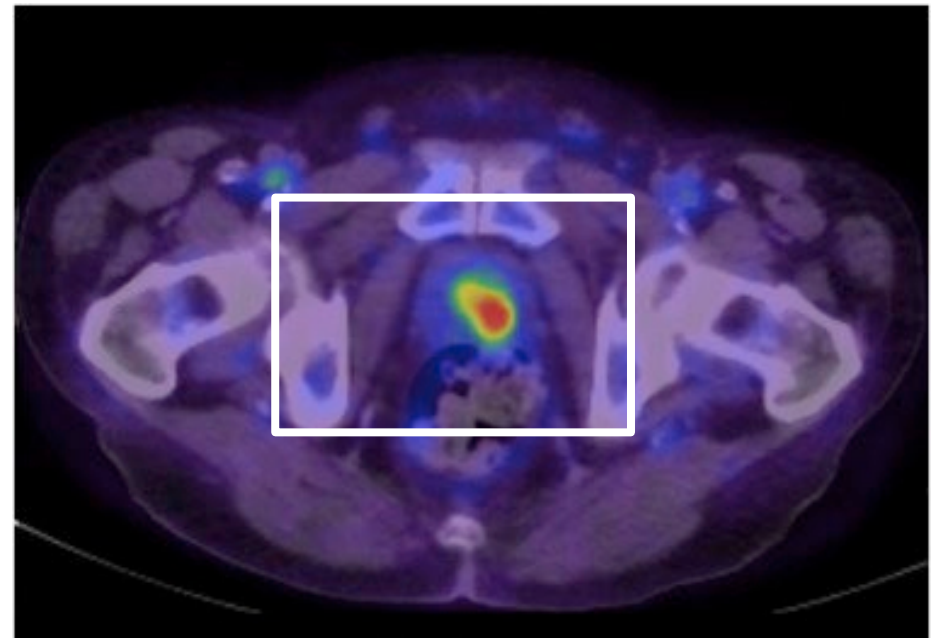
A. PSA: 149.0 ng/ml B. PSA: 44.99 ng/ml C. PSA: 40.0 ng/ml D. PSA: 148.0 ng/ml



What is a PET-CT scan?



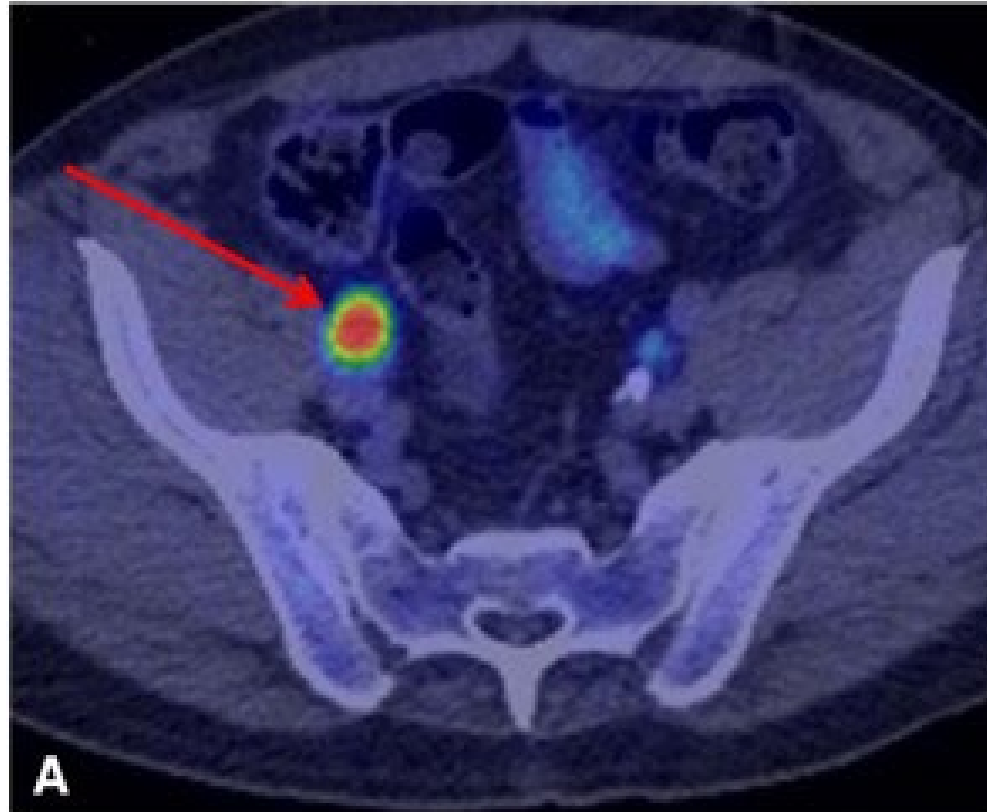
CT can give sharper
images of bone
structure etc



PET scan shows
cell activity NOT
seen on CT scan

What is a PET-CT scan?

Fusion of CT and
PET images of
the same patient



What is a PSMA scan?

Prostate

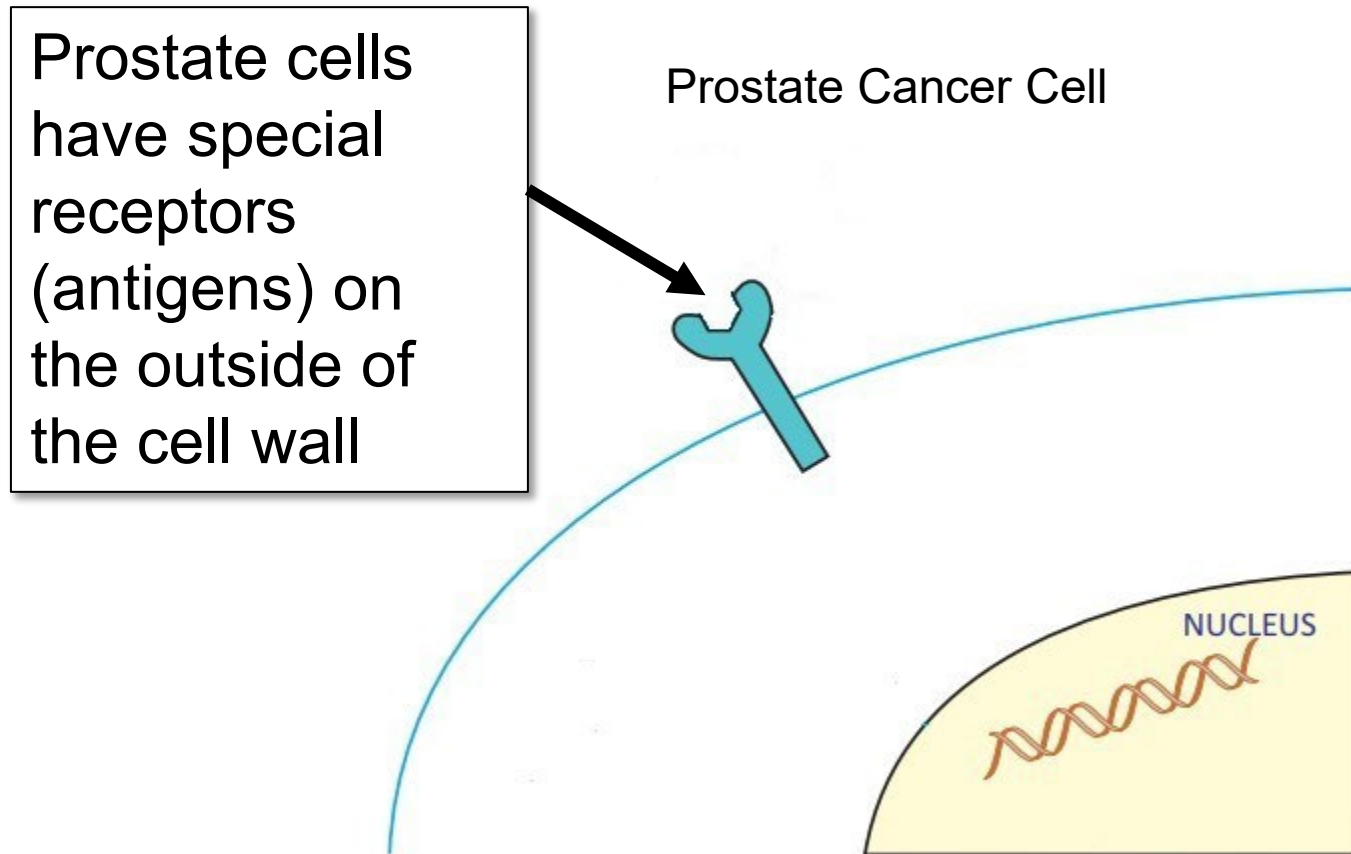
Specific

Membrane

Antigen

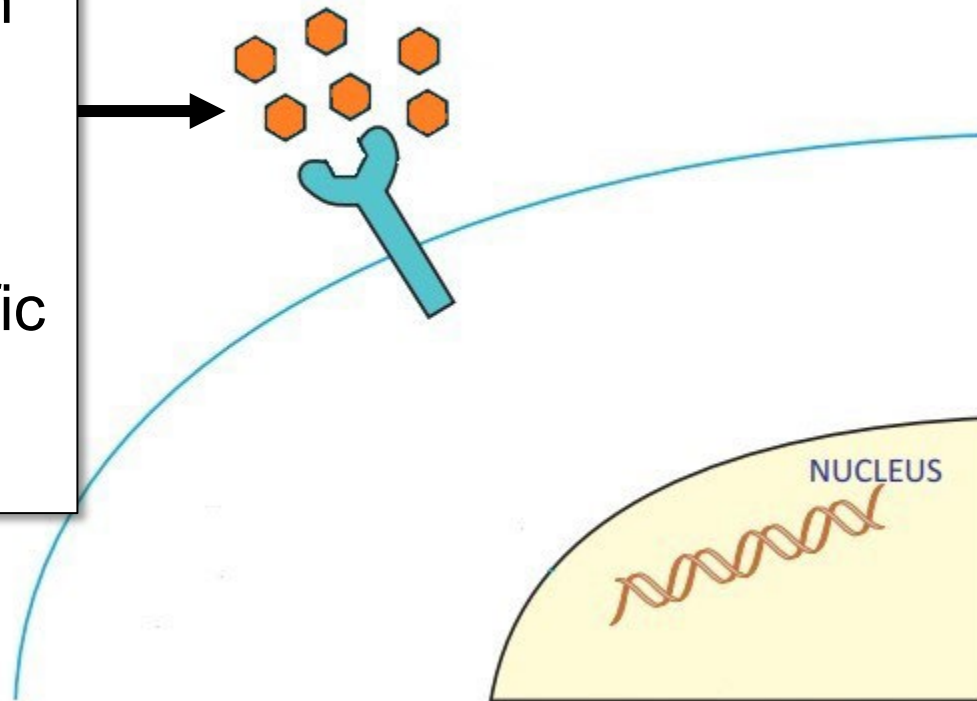
for 'antigen read 'receptor'

Prostate-specific membrane antigen

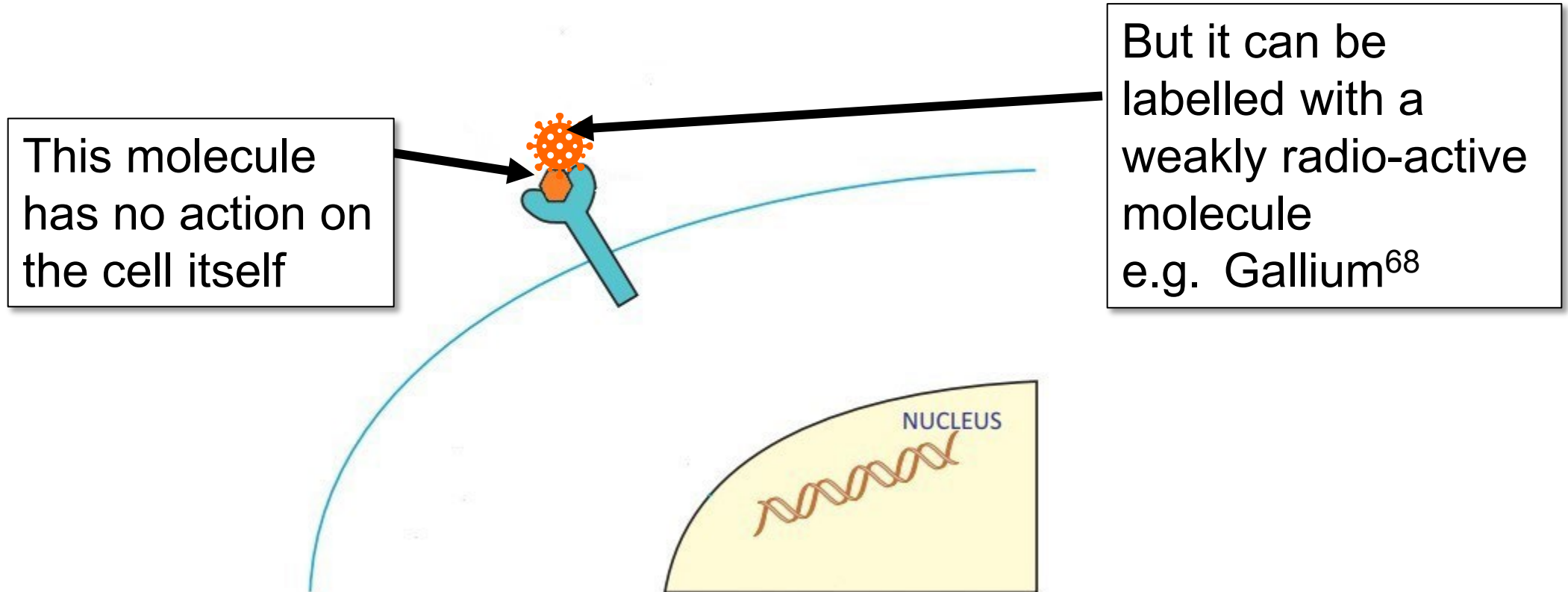


Prostate-specific membrane antigen

A molecule can be designed to specifically occupy the prostate-specific membrane antigen



Prostate-specific membrane antigen

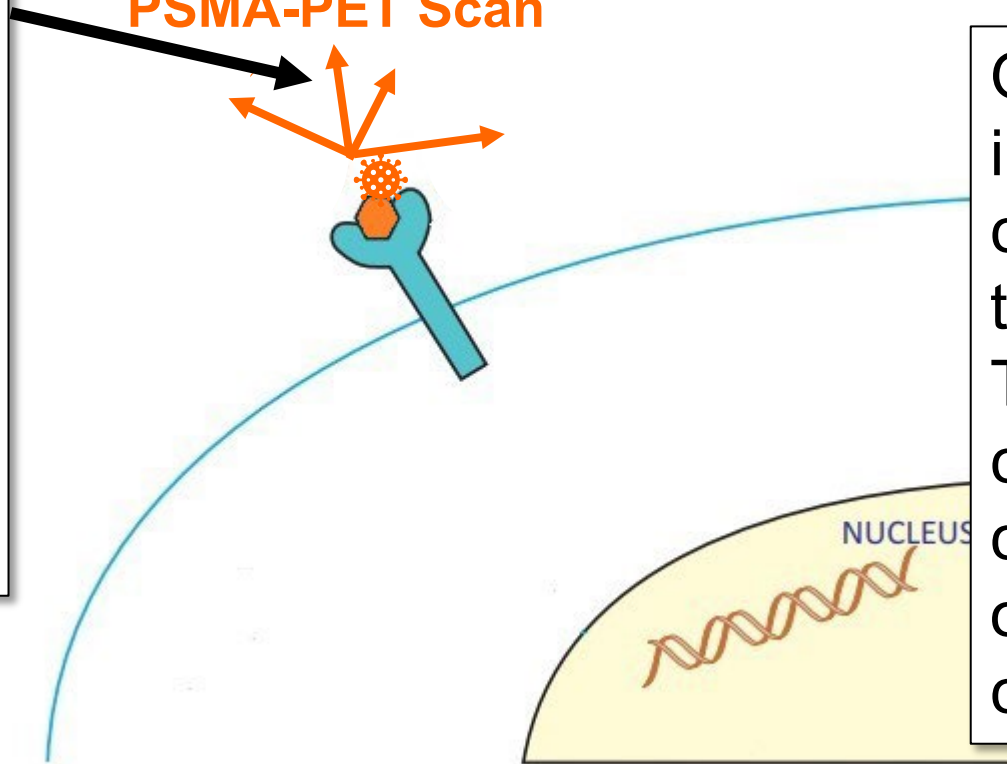


PSMA-PET CT SCAN

The Gallium⁶⁸ gives off 'positrons' as it decays

These can be identified with a PET scanner

PSMA-PET Scan



On the scan images, high concentrations of tracer will be seen. These will correspond to concentrated areas of prostate cancer cells.

Is this scan truly 'prostate specific'?

Well, not ***really***

Other tissues in the body can also pick up the tracer
but to a lesser extent

Liver, kidney, spleen, bone marrow (Salivary and lacrimal glands)

The term *prostate-specific* can be confusing

Is this scan truly 'prostate specific'?

PCa cells pick up the radio-tracer in greater concentration because of the very large number of receptors / antigens present:

100 to 1000 times more than on the other cells

Is this scan truly 'prostate specific'?

Treatment with hormone therapy (ADT) also increases the numbers of prostate-specific membrane antigens.

Thus PSMA scans for PCa secondaries become even more sensitive in patients who have been on hormone therapy.

Potentially of great value in non-metastatic hormone resistant PCa – (Biochemical recurrence)

Interpretation of PSMA-PET CT Scan

The 'art' of interpreting PSMA scans is to identify areas of high uptake where there shouldn't be any

Interpretation of PSMA Scan



- ← Injection site in vein
- ← Lacrimal glands
- ← Salivary glands

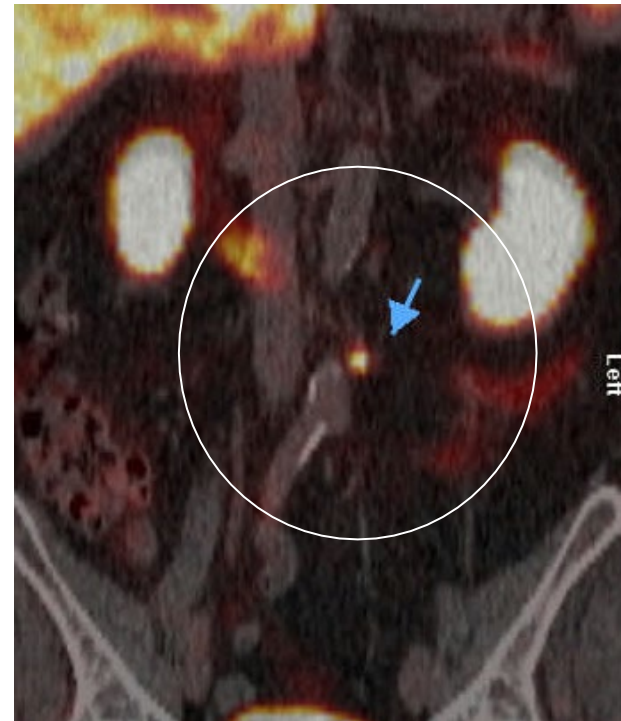
← Liver, kidney spleen etc

Interpretation of PSMA Scan

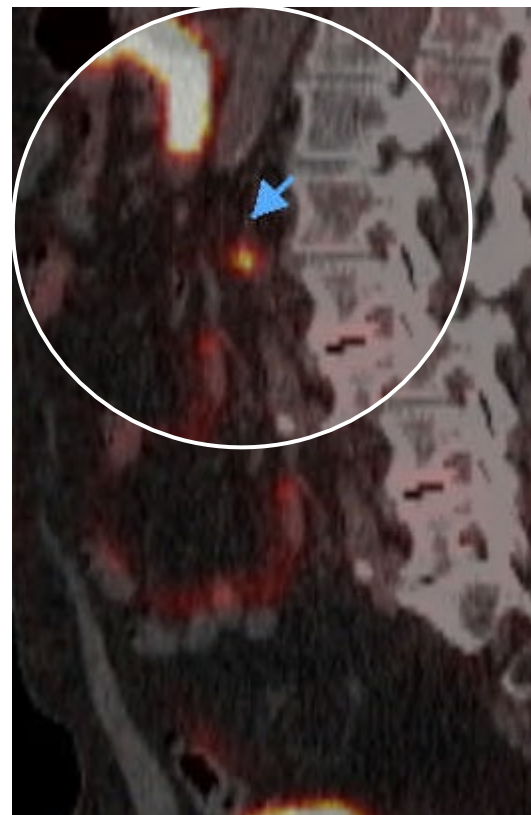


PSMA-PET CT Scan

Gives even better images



Interpretation of PSMA-PET CT Scan



Is PSMA better than PET alone?

PET:

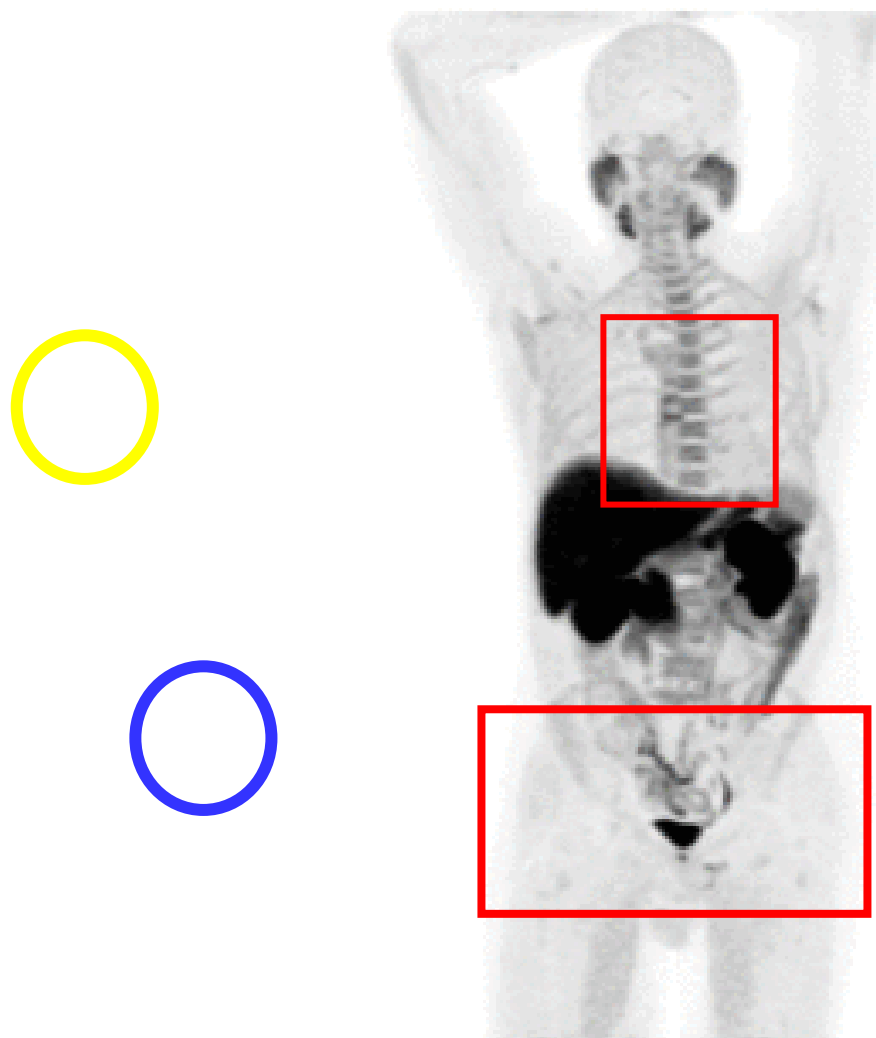
Useful from PSA 2.0 upwards?

PSMA-PET

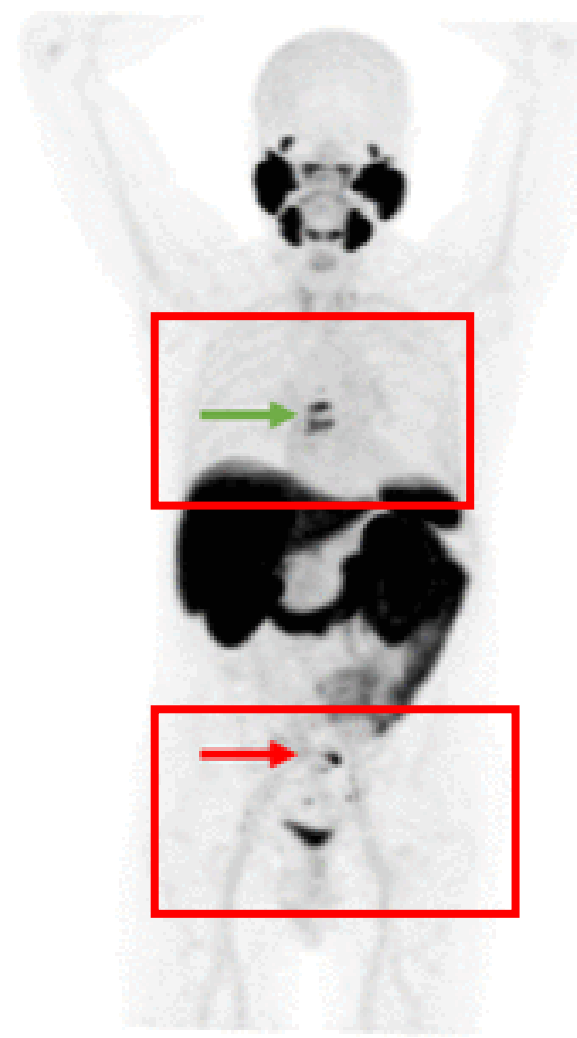
Starts becoming useful from PSA 0.2 – 0.3

Better from 0.5

Is PSMA better than PET alone?



^{18}F -fluorocholine PET



^{18}F -PSMA-1007 PET





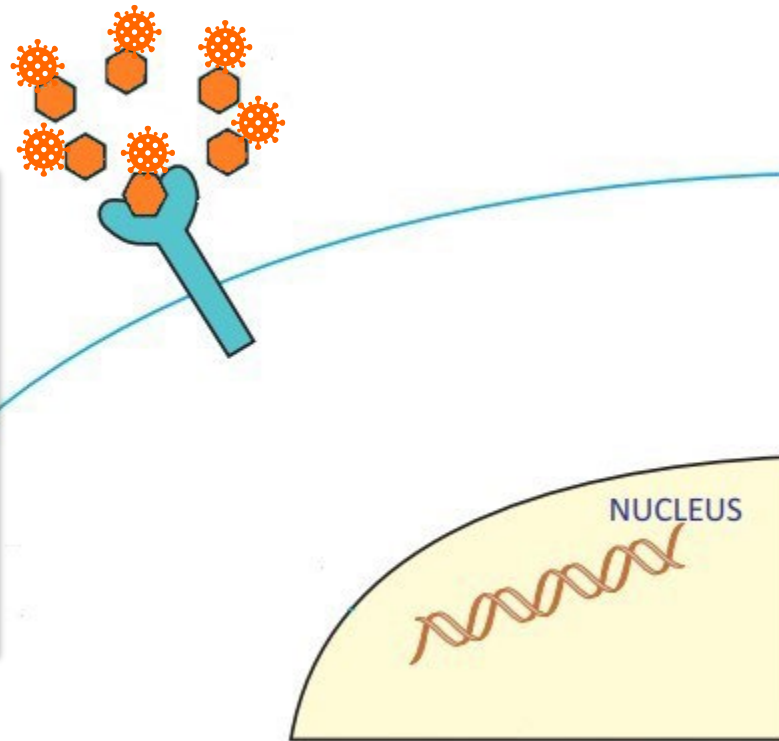
*"Can PSMA
technology be
used for
treatment?"*

YES

Radio-ligand therapy
Molecular Radiotherapy

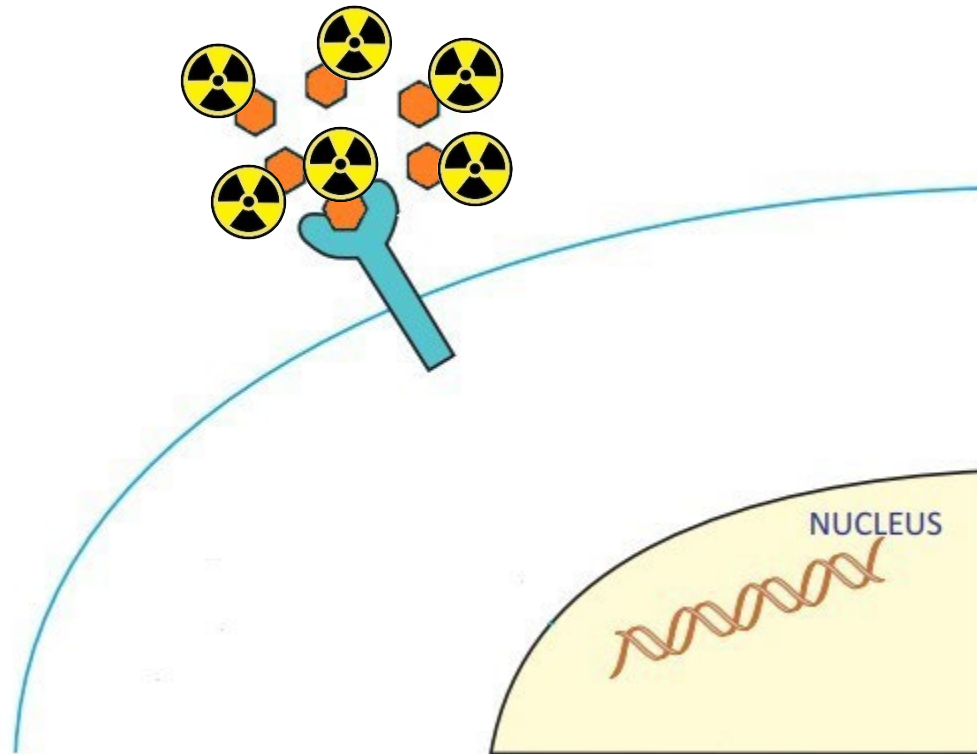
Radio-ligand therapy

This can be achieved by substituting the normal low-dose radio-active label ^{68}Ga Gallium



Radio-ligand therapy

A highly radioactive label is 'glued' to the carrier molecule.

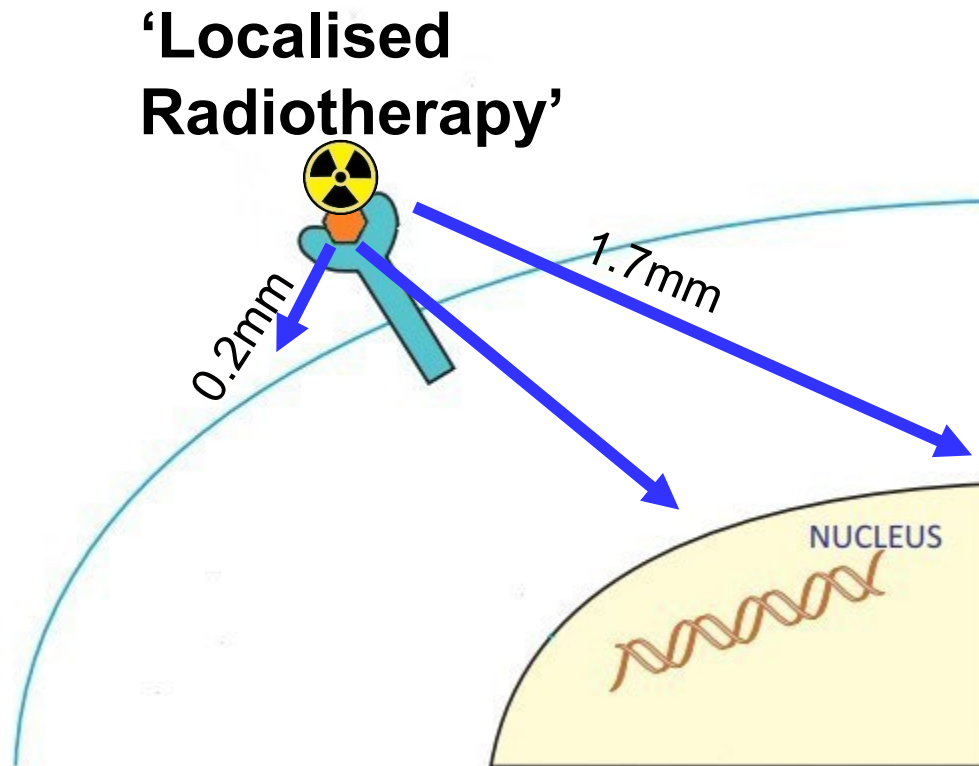


Radio-ligand therapy

The isotope gives off local radioactivity to damage the cancer cell

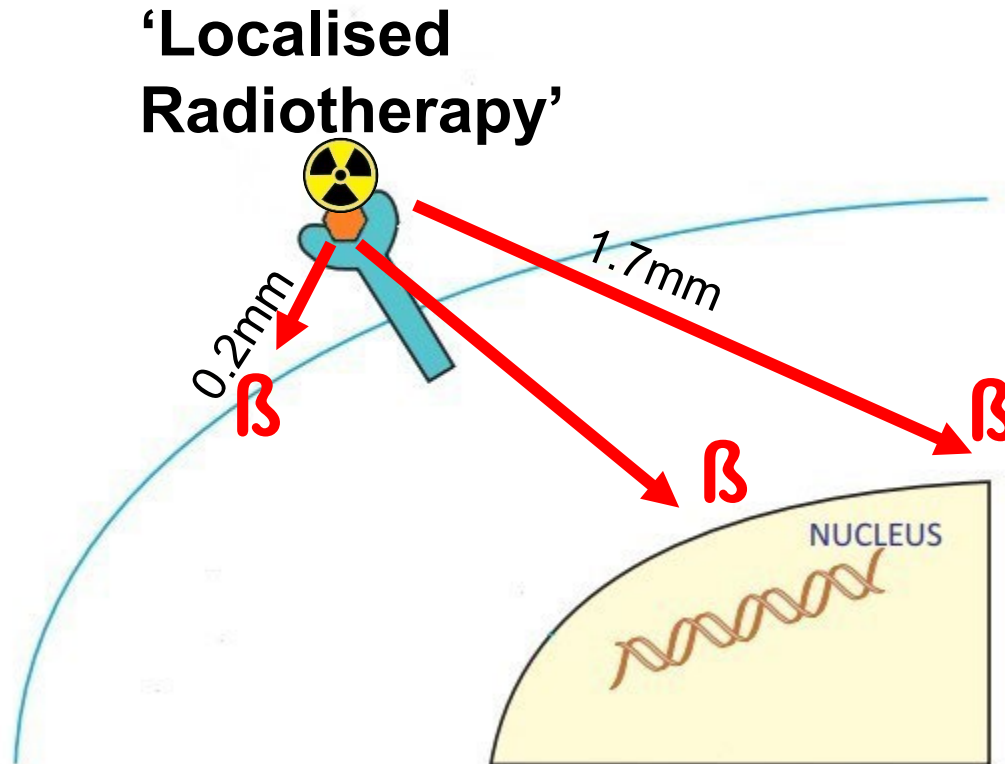
‘Localised radiotherapy’

‘Molecular radiotherapy’



Radio-ligand therapy

Degree of tissue damage depends on the radioactivity given off

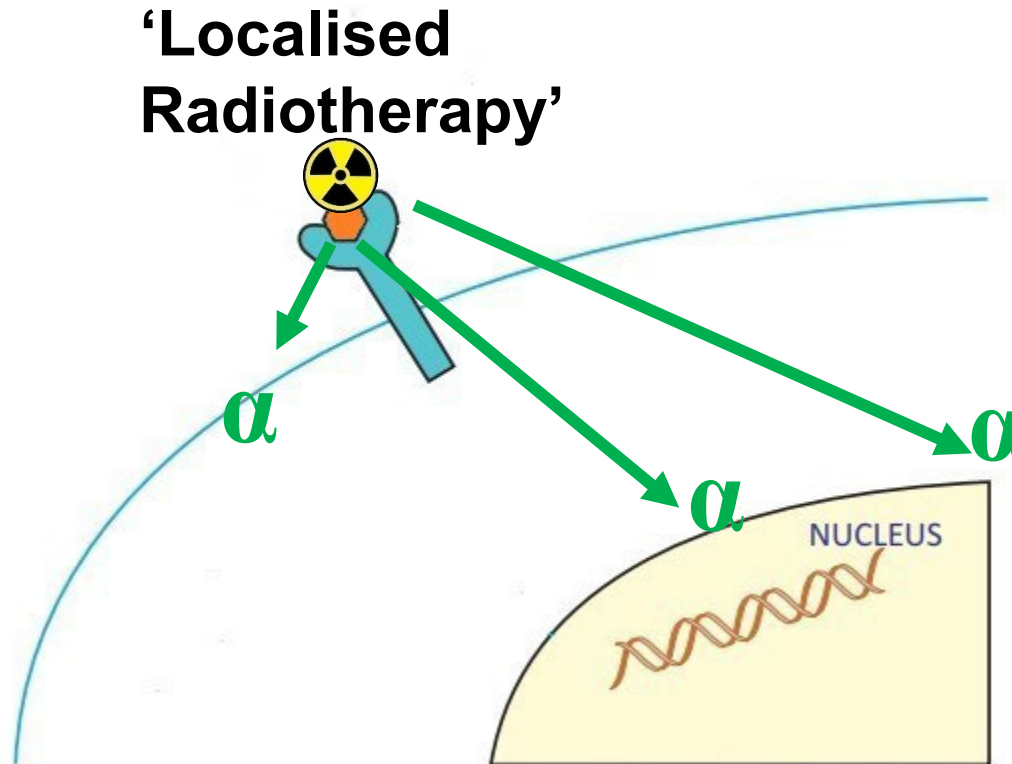


^{177}Lu Lutetium

β Particles

Radio-ligand therapy

Degree of tissue damage depends on the radioactivity given off



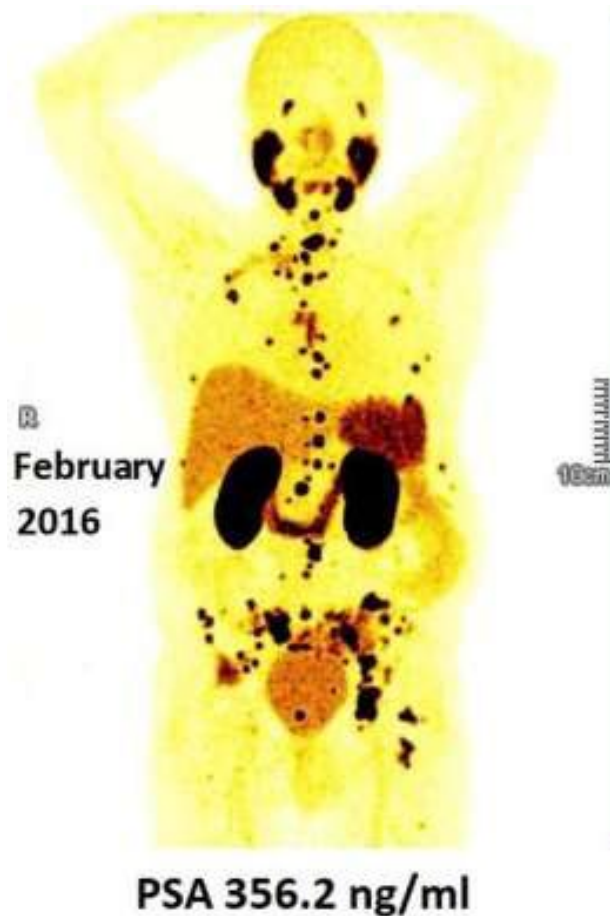
α particles

$^{225}\text{Actinium}$

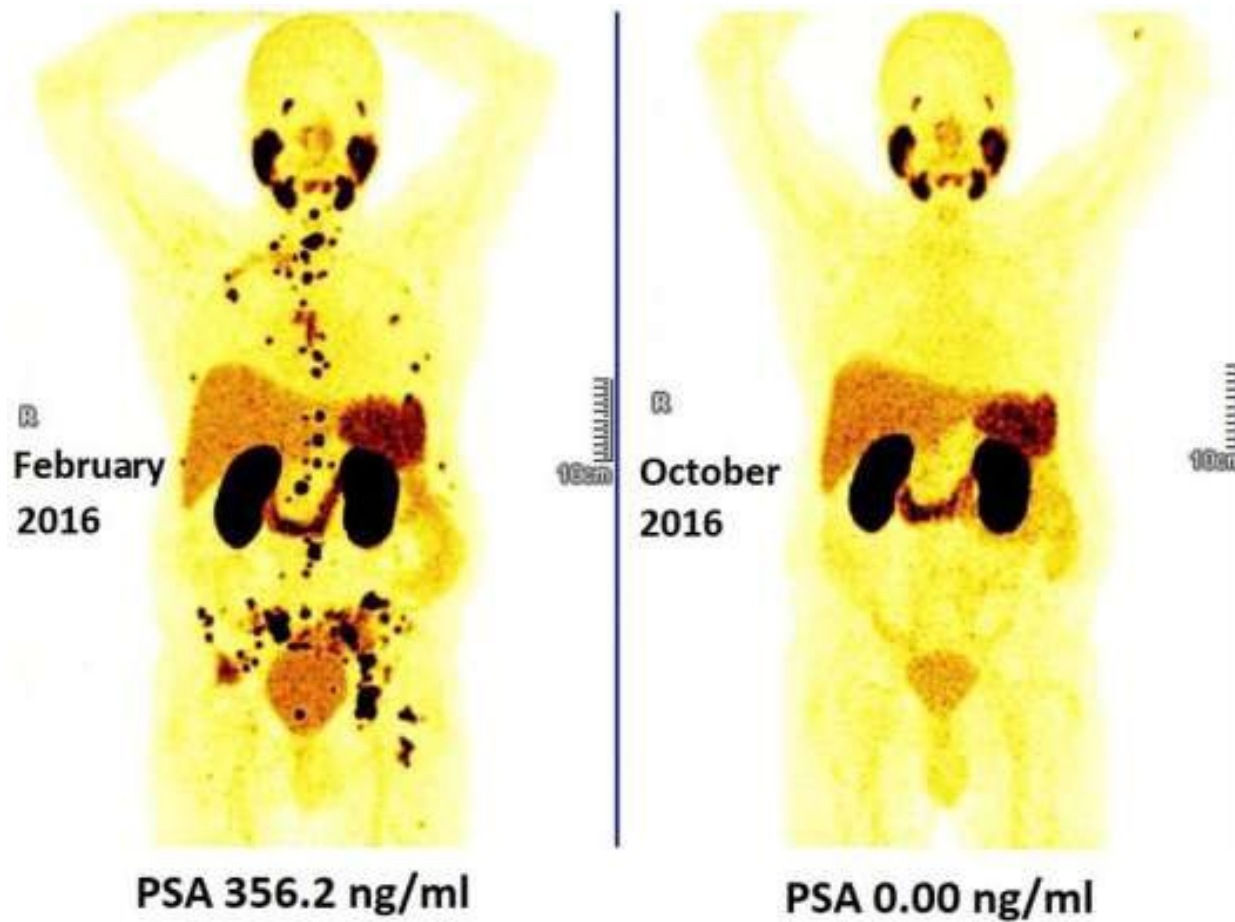
Higher energy particles

More localised action on tissues - ?
Less overall S/E
? Less effect on salivary glands

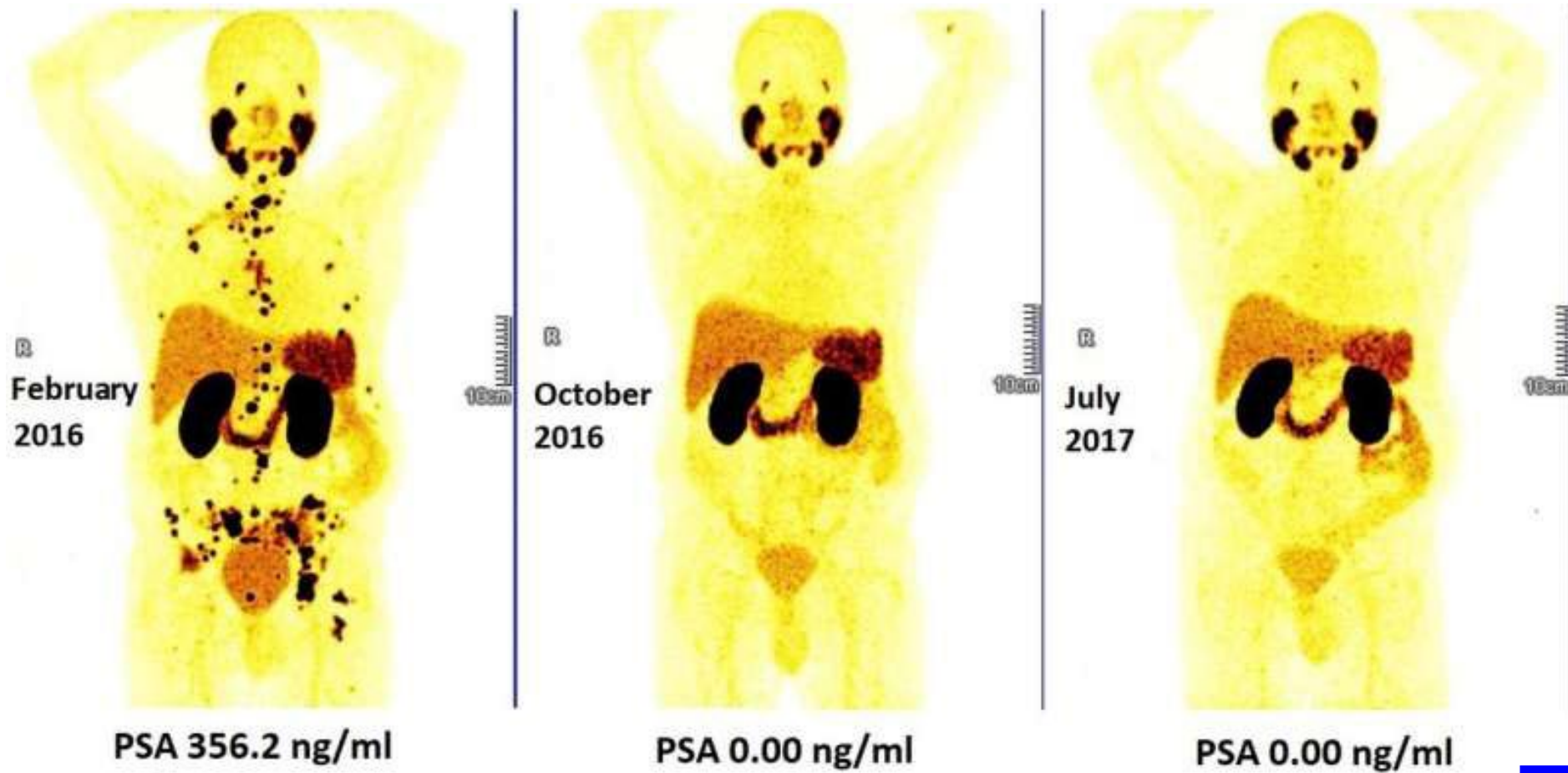
Lutetium¹⁷⁷ Radiotherapy

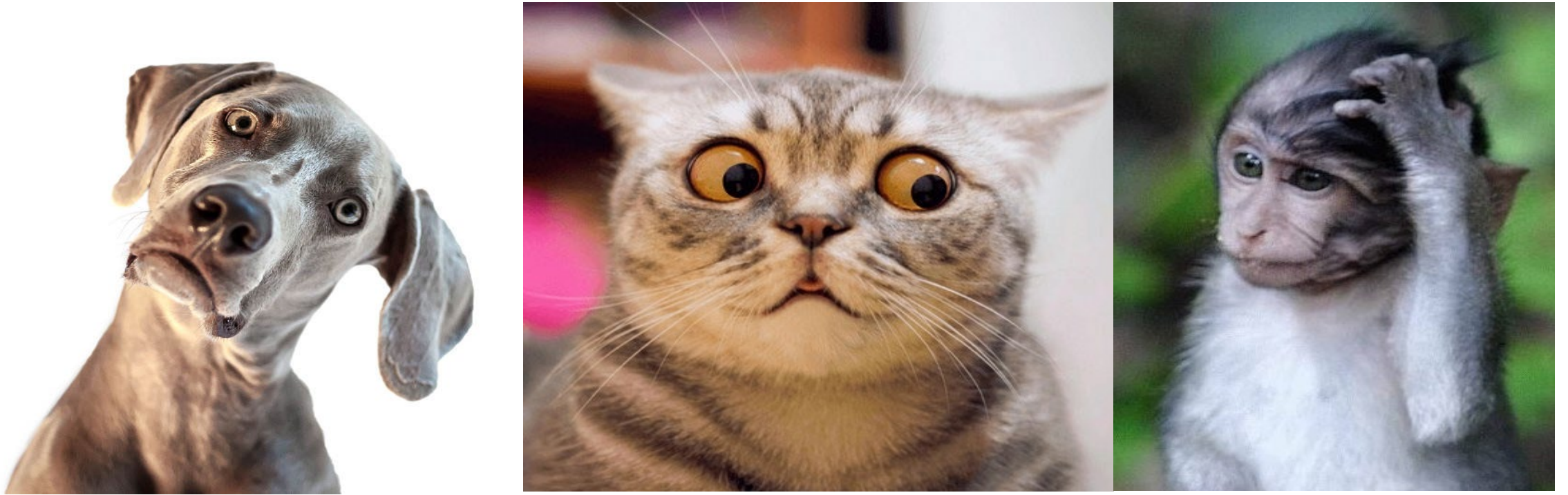


Molecular Radiotherapy



Molecular Radiotherapy





**Still confused??
Too much information??**

Any Questions



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