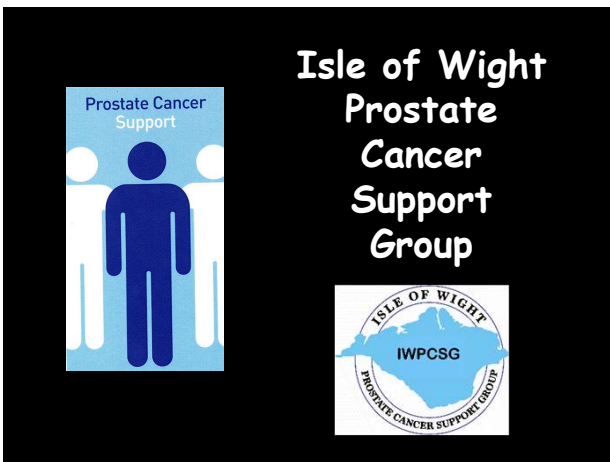


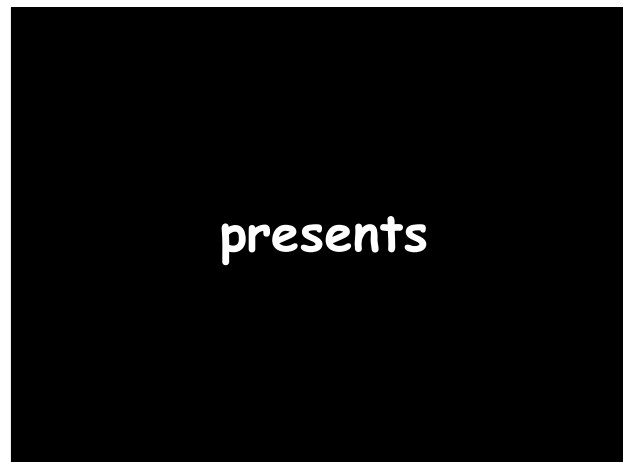
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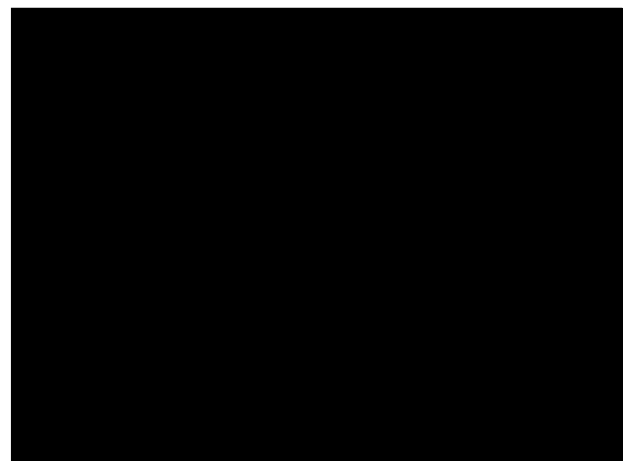
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6



7

Diagnosis has improved

Prostate Cancer

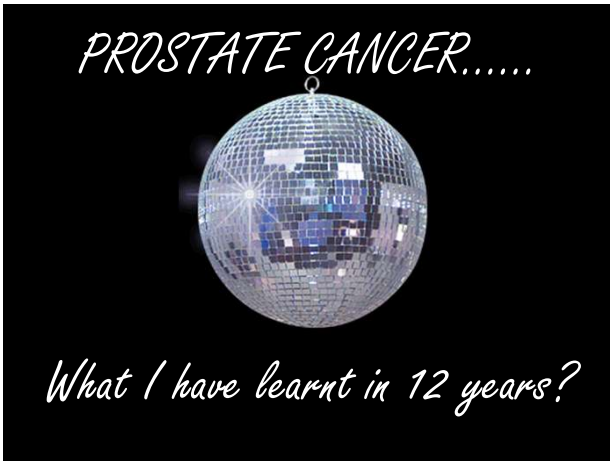
Looking through the lens of a patient - 12 years on

What about Diagnosis?

QUESTIONS ANSWERS

Some thoughts on 12 years of Prostate Cancer

10



8

The biggest game-Changer?

Prostate Cancer

Looking through the lens of a patient - 12 years on

The biggest Game-Changer

- Should be standard practice to scan before biopsy
- Now in the NICE guideline
- Biopsy rate reduced by 30%
- Targeted biopsy now easier

Some thoughts on 12 years of Prostate Cancer

11

Early Awareness is vital

Prostate Cancer

Looking through the lens of a patient - 12 years on

Increasing awareness

- Increasing awareness of disease is vital
- Awareness
- Diagnosis
- Investigation
- Treated
- Best outcome with early treatment

Some thoughts on 12 years of Prostate Cancer

9

Developments in Surgery

Prostate Cancer

Looking through the lens of a patient - 12 years on

Robotic / laparoscopic prostatectomy

- Now the norm for major surgery
- Any better than the open operation?
- Less bleeding
- Less incontinence?
- Less E DP
- Nerve sparing surgery

Some thoughts on 12 years of Prostate Cancer

12

Radiotherapy advances

Prostate Cancer

Looking through the lens of a patient - 12 years on

External beam RadioTx

- Linear accelerator
- Accurate beam shaping and dosage
- Fewer side effects and tissue damage

Some thoughts on 12 years of Prostate Cancer

13

What does the future hold?



What else is there to come?

16

New drug therapies

Prostate Cancer

Looking through the lens of a patient - 12 years on

Other forms of ADT

- Hormone resistant prostate cancer
- Abiraterone (2011) - stops body producing testosterone (different action to Zoledronic acid)
- Enzalutamide (2012) - blocks the action of testosterone (or other cells)

Some thoughts on 12 years of Prostate Cancer

14

PROSTATE CANCER

WHAT IS IT ALL ABOUT?

WHAT ARE THE IMPORTANT FACTS?

17

How can a Support Group help?

Prostate Cancer

Looking through the lens of a patient - 12 years on

SUPPORT MATTERS

CONTACT DETAILS

The Reading Prostate Cancer Support Group

Some thoughts on 12 years of Prostate Cancer

15

WHAT IS NEW?

HOW HAVE THINGS MOVED ON?

18

Fact

Prostate Cancer is the most common cancer in men in UK

TRUE
42,975 diagnosed in 2016/17

National Prostate Cancer Audit 2018 Published Feb 2019

19

True or False?

mpMRI should be performed *before* prostate biopsy

TRUE
Now part of NICE Guideline 2019

NICE Guideline CG 175 (published 2019)

22

True or False?

We are improving early diagnosis of Prostate Cancer

FALSE
Only 45% men have localised disease at diagnosis

National Prostate Cancer Audit 2018 Published Feb 2019

20

Fact

Early curative treatment saves money

TRUE
Early Rx €15,000
Advanced disease €300,000

Wu, B et al: J Clin Oncol. 2018.36(suppl):88

23

Fact

Active Surveillance is a proven safe option in low grade Prostate Cancer

TRUE
Improved monitoring gives good outcomes

Hamdy, FC et al: NEJM. 2016. 375: 1415-24

21

True or False?

Every man needs a biopsy for the diagnosis of Prostate Cancer

FALSE
mpMRI has reduced biopsy rate by >30%

National Prostate Cancer Audit 2018 Published Feb 2019

24

True or False?

We are still significantly over-treating low-risk Prostate Cancer

FALSE
4%
2016/17
8%
2015/16

National Prostate Cancer Audit 2018. Published Feb 2019

25

Prostate Cancer

Looking through the lens of a patient - 12 years on

28

Commonly held opinion

The PSA test is 'unreliable' or 'inaccurate'

FALSE
Sensitive & Specific but not Selective for PCa

Royal College of GPs, March 2018

26

Some personal thoughts....

....and some new information

FACTS

29

True or False?

Men with Prostate Cancer feel they are being treated well

TRUE
90% men rated care as 8/10 overall

National Prostate Cancer Audit 2018. Published Feb 2019

27

PAST

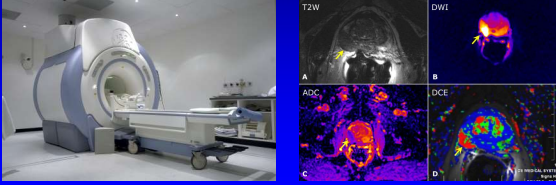
FUTURE

What do I think are the most tangible changes over the past 12 years?
What's new in prostate cancer?

30

The biggest Game-Changer

- Multiparametric MRI
 - ‘Sees inside the prostate’



31

A Useful Spin-Off

- PSA Density
 - mpMRI can now accurately measure prostate volume
 - PSA and prostate volume ratio computed


High PSA and large prostate volume – Low PD
Mildly raised PSA and moderate prostate volume – Normal PD
High PSA and low prostate volume – High PD

PSA Density may be as useful as Gleason score – particularly in PSA range 4 – 10ng/ml

34

The biggest Game-Changer

- Should be standard practice to scan before biopsy
- Now in the NICE guideline
- Biopsy rate reduced by 30%
- Targeted biopsy now easier



32

What's new in treatment?

35

The biggest Game-Changer


- Should be standard practice to scan before biopsy
- Now in the NICE guideline
- Biopsy rate reduced by 30%
- Targeted biopsy now easier



33

Robotic / laparoscopic prostatectomy


- Now the norm for major surgery
- Any better than the open operation?
 - Less bleeding
 - Less incontinence?
 - Less E D?
 - Nerve sparing surgery



36

Robotic / laparoscopic prostatectomy

- NPCA Audit 2019 (April 2017 – March 2018)
- 7, 018 Radical surgery
 - 85% Robotic
 - 6% Laparoscopic
 - 8% Open

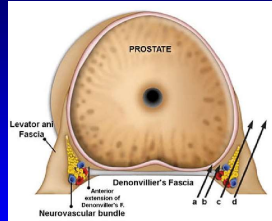


37

Robotic / laparoscopic prostatectomy

- ‘NeuroSAFE’

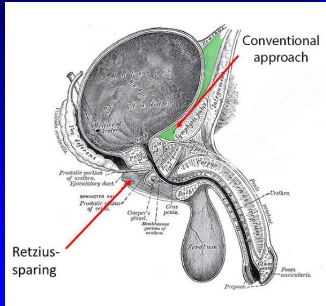
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40

Robotic / laparoscopic prostatectomy

- ‘Retzius Sparing’ surgical technique

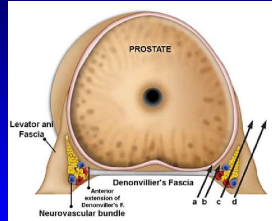


38

Robotic / laparoscopic prostatectomy

- ‘NeuroSAFE’

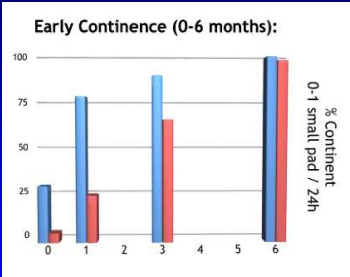
Neurovascular
Structure
Adjacent
Frozen section
Examination



41

Reading results

Early Continence (0-6 months):



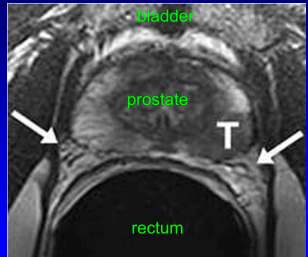
Number of Pads	Robotic Approach (%)	Conventional Approach (%)
0	~25	~5
1	~75	~25
2	~85	~65
3	~90	~75
4	~95	~85
5	~98	~95
6	~100	~100

39

Robotic / laparoscopic prostatectomy

- ‘NeuroSAFE’

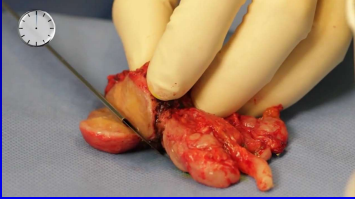
Neurovascular
Structure
Adjacent
Frozen section
Examination



42

Robotic / laparoscopic prostatectomy

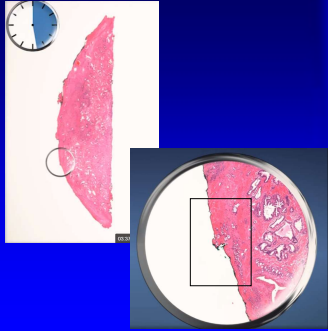
- 'NeuroSAFE'
- N**eurovascular
- S**tructure
- A**djacent
- F**rozen section
- E**xamination



43

Robotic / laparoscopic prostatectomy


- 'NeuroSAFE'
- N**eurovascular
- S**tructure
- A**djacent
- F**rozen section
- E**xamination



46

Robotic / laparoscopic prostatectomy


- 'NeuroSAFE'
- N**eurovascular
- S**tructure
- A**djacent
- F**rozen section
- E**xamination



44

Robotic / laparoscopic prostatectomy

- 'NeuroSAFE'
- N**eurovascular
- S**tructure
- A**djacent
- F**rozen section
- E**xamination




Men are being diagnosed earlier.
Side effects are very important concern when choosing treatment

47

Robotic / laparoscopic prostatectomy

- 'NeuroSAFE'
- N**eurovascular
- S**tructure
- A**djacent
- F**rozen section
- E**xamination



45

Robotic / laparoscopic prostatectomy

- 'NeuroSAFE'
- N**eurovascular
- S**tructure
- A**djacent
- F**rozen section
- E**xamination



Very limited availability on NHS

Men are being diagnosed earlier.
Side effects are very important concern when choosing treatment


48

External beam RadioTx

49

External beam RadioTx


- IMRT **IG-IMRT**
 - Image guided Intensity modulated Radiotherapy
- CT localisation at the time of treatment
 - No need to rely on skin markers alone
- Hypofractionation



52

External beam RadioTx


- Linear accelerator 3D-CRT
 - 3D Conformal RadioTherapy
- Accurate beam shaping
- Fewer side effects and tissue damage



50

External beam RadioTx



- NPCA Audit 2019 (April 2017 – March 2018)
- 13,891 Radiotherapy
 - 90% IMRT / IG-IMRT
 - 10% 3D Conformal



53

External beam RadioTx

- IMRT
 - Intensity Modulated Radiotherapy
- Accurate beam shaping and variable dosage
- Shorter Rx cycles
 - 'Hypofractionation'

51

Stereotactic Ablative Radiotherapy (SABR)

- Even more focused and accurate dosage
 - Multiple narrow focussed radiation beams from multiple directions
 - ✦ Can compensate for patient movement and breathing
- Not widely available on NHS

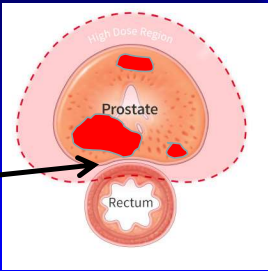


CyberKnife™
Varian® Elekta®

54

External beam RadioTx

- Need to minimise collateral damage to rectum
- Increase space between prostate and rectum

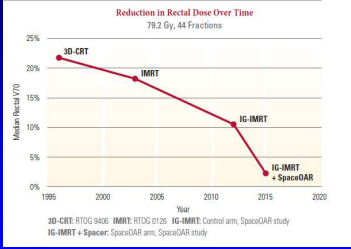


The diagram shows a cross-section of the prostate and rectum. A red shaded area labeled 'High Dose Region' encompasses the prostate. An arrow points to the gap between the prostate and the rectum, indicating the goal of increasing this space to reduce radiation exposure to the rectum.

55

SpaceOAR

- Significantly reduces radiation dose to rectum
- 'Ultra hypo fractionation' 5 sessions of Rx may be the norm and not 20



Reduction in Rectal Dose Over Time
79.2 Gy, 44 Fractions

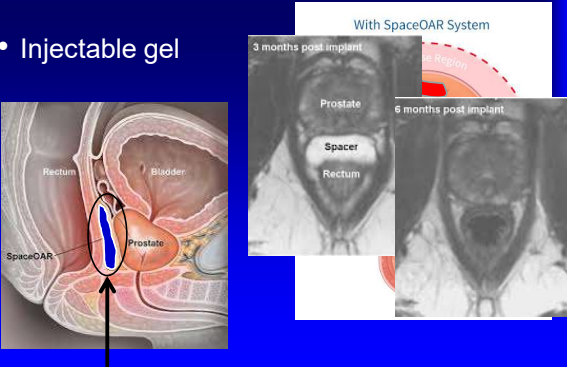
Year	3D-CRT	IMRT	IG-IMRT	IG-IMRT + SpaceOAR
1995	~22%	-	-	-
2000	~20%	-	-	-
2005	~18%	~18%	-	-
2010	-	-	~10%	-
2015	-	-	-	~5%

Legend: 3D-CRT: RTG 8450; IMRT: RTG 0126; IG-IMRT: Control arm, SpaceOAR study; IG-IMRT + SpaceOAR: SpaceOAR arm, SpaceOAR study

58

SpaceOAR

- Injectable gel

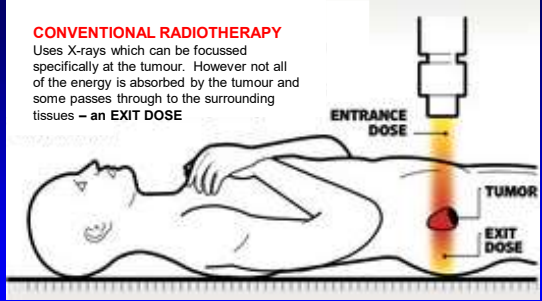


The anatomical diagram shows the rectum, bladder, and prostate, with the SpaceOAR gel (blue) injected between the prostate and rectum. The MRI scans show the 'With SpaceOAR System' at 3 months and 6 months post-implant, with labels for Prostate, Spacer, and Rectum.

56

Proton beam therapy

CONVENTIONAL RADIOTHERAPY
Uses X-rays which can be focussed specifically at the tumour. However not all of the energy is absorbed by the tumour and some passes through to the surrounding tissues – an EXIT DOSE

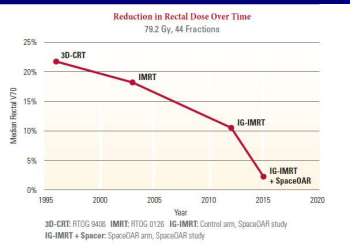


The diagram shows a patient lying on a table. A beam of X-rays enters from the top, passes through the body, and exits at the bottom. The entrance dose is shown as a yellow beam, and the exit dose is shown as a red beam. The tumor is located in the middle of the body.

59

SpaceOAR

- Significantly reduces radiation dose to rectum
- 'Ultra hypo fractionation' 5 sessions of Rx may be the norm and not 20



Reduction in Rectal Dose Over Time
79.2 Gy, 44 Fractions

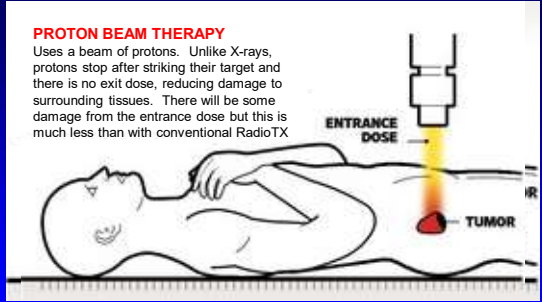
Year	3D-CRT	IMRT	IG-IMRT	IG-IMRT + SpaceOAR
1995	~22%	-	-	-
2000	~20%	-	-	-
2005	~18%	~18%	-	-
2010	-	-	~10%	-
2015	-	-	-	~5%

Legend: 3D-CRT: RTG 8450; IMRT: RTG 0126; IG-IMRT: Control arm, SpaceOAR study; IG-IMRT + SpaceOAR: SpaceOAR arm, SpaceOAR study

57

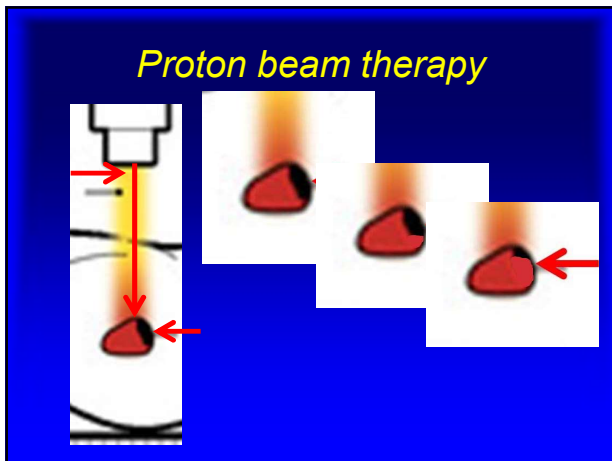
Proton beam therapy

PROTON BEAM THERAPY
Uses a beam of protons. Unlike X-rays, protons stop after striking their target and there is no exit dose, reducing damage to surrounding tissues. There will be some damage from the entrance dose but this is much less than with conventional RadioTX

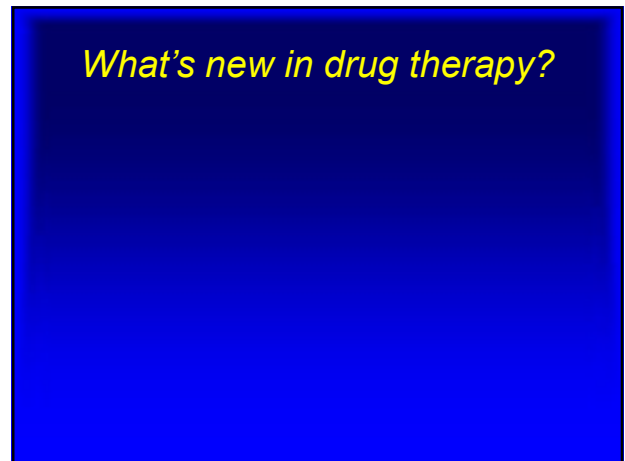


The diagram shows a patient lying on a table. A beam of protons enters from the top, passes through the body, and stops at the tumor. The entrance dose is shown as a yellow beam, and there is no exit dose. The tumor is located in the middle of the body.

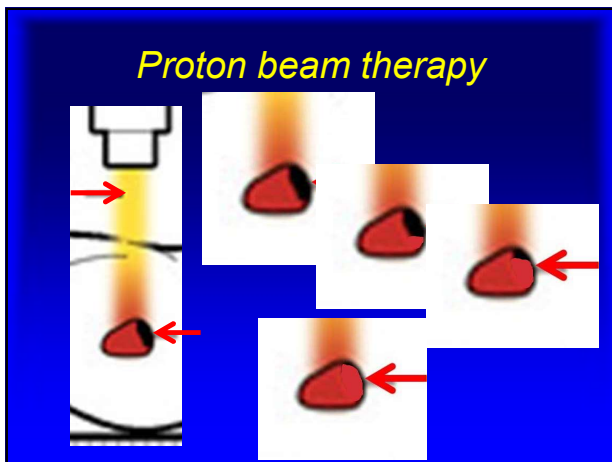
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61



64



62

Androgen Deprivation Therapy

- 'Hormone resistant prostate cancer'
- Abiraterone (2011) – stops body producing testosterone (different action to Zoladex)
- Enzalutamide (2012) – blocks the action of testosterone on cancer cells

Two images of medicine bottles: Zytiga (abiraterone) and Xtandi (enzalutamide).

65

Localised therapy

- HIFU - High Intensity focussed ultrasound
- Cryotherapy
- Vascular targeted photodynamic therapy

None approved by NICE

63

Newer drug therapy

- 'Hormone resistant prostate cancer'
- Abiraterone (2011) – stops body producing testosterone (different action to Zoladex)
- Enzalutamide (2012) – blocks the action of testosterone on cancer cells

? Use earlier in treatment pathway – not just for life extension where all else has failed

An image of Xtandi (enzalutamide) medicine bottles.

66

Newer drugs

- Apalutamide
- Darolutamide



67

Combination therapy

- A combination of hormone therapy and chemo or drug therapy
 - ? Abiraterone
 - ? Enzalutamide
- Patients unable to have chemo with docetaxel



70

Combination therapy

68

Combination therapy


- Newly diagnosed metastatic hormone sensitive PCa
- 17% newly diagnosed men
 - many in younger age group
 - often asymptomatic



71

Combination therapy

- A combination of hormone therapy and chemo or drug therapy
 - Chemotherapy now being used earlier in treatment pathway
 - Patients with metastases at diagnosis
 - ? Compare with other cancers



69

Gene Therapy for PCa

72

Gene Therapy for PCa

- This is not about physically altering the genes themselves
- Concerns the ability of cells to repair their genes when damaged at cell division



73

PARP

- NOT



"The hooter on Noddy's car made a loud 'parp' to let Big Ears know he was waiting..."

76

Gene Therapy for PCa

- This occurs in both normal and cancerous cells
- Interfering with the repair process prevents the cell for multiplying



74

PARP

- NOT



"The hooter on Noddy's car made a loud 'parp' to let Big Ears know he was waiting..."

77

Selective Gene Therapy

- The ability to selectively interfere with repair mechanisms *only* in cancerous cells
 - 'Synthetic lethal effect'
- Selective gene therapy can stop cancerous cells from multiplying but not normal ones



"Targeted Gene Therapy"

75

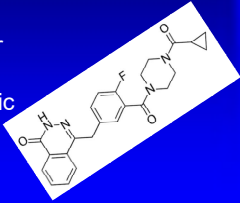
PARP

- Poly (**A**D**P**-**R**ibose) Polymerase
- Enzyme system associated with cell repair mechanisms
- Drugs which interfere with PARP will affect cell division and growth
 - 'PARP Inhibitors'

78

Olaparib


- This is one of a new class of drugs
 - ‘PARP’ inhibitors
- Specifically targets the repair mechanisms in cancer cells of patients with known genetic abnormalities
 - first used in advanced breast cancer



79

Additional therapy

- Non-metastatic castrate resistant prostate cancer
- Non-metastatic hormone relapsed prostate cancer
- ‘Biochemical recurrence’ of prostate cancer

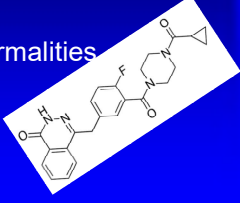


An ‘unmet need’

82

Olaparib


- BRCA 1 & BRCA 2
 - Commonest genetic defects in PCa
 - Also associated with breast cancer
- Many other genetic abnormalities
 - ATM
 - 12 others



80

Additional therapy

- Relaxation needed of current rules of use of additional drugs
- Earlier use of more sensitive scanning techniques




An ‘unmet need’

“We know my cancer is growing – my PSA is going up. Why do I have to wait until it is too late for treatment to be started?”

83

Olaparib

- Olaparib is effective in prolonging survival in men with BRCA 1&2, ATM genetic abnormalities
 - BRCA 2 is the most common abnormality
 - Some evidence of benefit in other genetic abnormalities.
 - Waiting for NICE approval




81

What’s new in imaging?

84

Improved imaging


- PET - **P**ositron **E**mission **T**omography
 - Demonstrates cell activity
- F¹⁸ FDG
 - ↪ fluorodeoxyglucose



85

Improved imaging

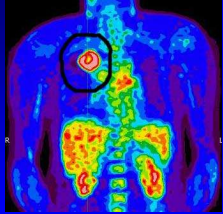
- PSMA PET scanning
- **P**rostate **S**pecific **M**embrane **A**ntigen
 - Ga⁶⁸ injection



88

Improved imaging

- PET - **P**ositron **E**mission **T**omography
 - Demonstrates cell activity
- F¹⁸ FDG
 - ↪ fluorodeoxyglucose
- C¹¹ choline
 - ↪ important in making cell walls
 - ↪ More sensitive for PCa cells
 - Not easy to manufacture
 - Occasional supply problems

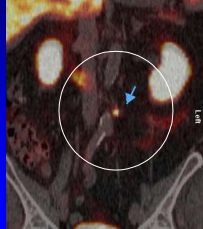


86

Improved imaging

PET Scanning


- PMSA PET scanning
 - Ga⁶⁸ injection



89

Improved imaging

- PSMA PET scanning
- **P**rostate **S**pecific **M**embrane **A**ntigen
 - Ga⁶⁸ injection

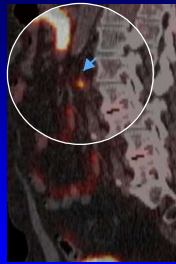


87

Improved imaging

PET Scanning

- PMSA PET scanning
 - Ga⁶⁸ injection

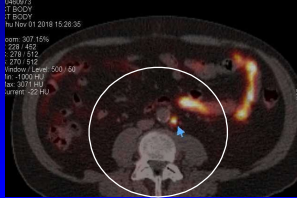


90

Improved imaging

PET Scanning

- PMSA PET scanning
 - Ga⁶⁸ injection

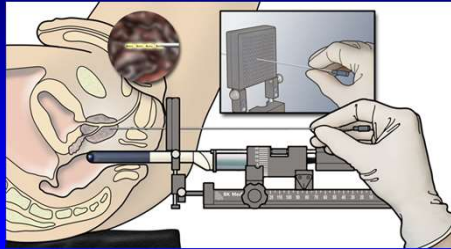


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 tar: 3071518
 server: 252.HU

91

Prostate biopsy

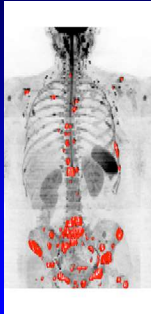
- Template biopsy



94

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



92

Prostate biopsy

- Targeted T-P Biopsy
 - LA procedure
 - All biopsies taken through 2 skin punctures



95

Prostate biopsy


- Trans-Rectal Ultrasound Guided
 - TRUS biopsy
 - Standard biopsy for most people
- Trans-Perineal Biopsy
 - Template biopsy
 - Targeted T-P biopsy

93

Prostate biopsy

- Targeted T-P Biopsy
 - LA procedure
 - All biopsies taken through 2 skin punctures

'Clean' puncture area
 Less infection risk
 Virtually zero
 incidence of sepsis



96

Theranostics

1 THERANOSTICS

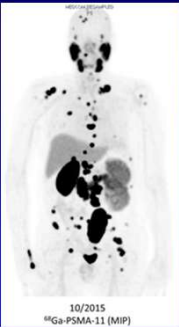
The use of techniques for diagnosis and purpose of treatment

DIAGNOSTICS

97

Theranostics

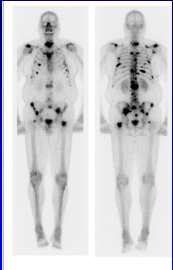
- Diagnostic technique:
 - ⁶⁸Gallium PSMA PET scanning
 - ⁶⁸Gallium attaches to prostate cell membranes – both in the prostate and secondaries
 - Bone and lymph nodes



100

Theranostics


- Diagnostic technique:
 - Bone scanning using radioactive labelled Technetium
 - taken up by all bone cells but concentrated in areas of highest bone cell activity e.g. cancer deposits



98

Theranostics

- Therapy technique:
 - Lutetium injection
 - ¹⁷⁷ Lutetium
 - Again attaches to prostate cell membranes
 - Releases therapeutic dose of radiation in very localised / targeted areas.




101

Theranostics

- Therapy technique:
 - Radium 223 injection


Taken up by bone cells in the same way as Technetium
Dosage is calculated to be sufficient to kill the cancer cells but not all of the normal bone cells which should then regenerate



99

Theranostics

- Therapy technique:
 - Lutetium injection



102

Theranostics

- Therapy technique:
 - Lutetium injection

103

What has NOT progressed well?

- Awareness
 - Patients
 - GPs
 - High Risk groups

106

Theranostics

- Therapy technique:
 - Lutetium injection

104

What has NOT progressed well?

- Awareness
 - In over 50% men the cancer has already spread outside the prostate capsule at the time of diagnosis

Men are still coming for testing too late

107

Theranostics

- Therapy technique:
 - Lutetium injection

105


The 'Bête Noire'?

- PSA test
- Remains contentious and confusing to many
 - Is it 'inaccurate' and 'unreliable'?
 - Too many people giving the wrong message

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The 'Bête Noire'?

- PSA test
- Remains contentious and confusing to many
 - Is it 'inaccurate' and 'unreliable'?
- Reduced rate of testing



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How is Prostate Cancer diagnosed?


The PSA test

- This is a blood test that measures the total amount of prostate specific antigen (PSA) in your blood. **SENSITIVITY**
- PSA is a protein produced by normal cells in the prostate and also by prostate cancer cells. No other chemical gives a positive result **SELECTIVITY**
- A **raised PSA will NOT have PCa** **SPECIFICITY**
- A **normal PSA WILL have PCa**

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The 'Bête Noire'?

- PSA test
- Remains contentious and confusing to many
 - Is it 'inaccurate' and 'unreliable'?
- What are the facts?



110

How is Prostate Cancer diagnosed?

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- PSA is a protein produced by normal cells in the prostate and also by prostate cancer cells. No other chemical gives a positive result **SELECTIVITY**
- A raised PSA level may show that you have a problem with your prostate, but not necessarily prostate cancer. **SPECIFICITY**

Rate of change of levels is more important than one absolute value **VARIABILITY**

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A few important facts...

- PSA based screening trials have reduced mortality by up to 64%

Hugusson J et al, Scand J Urol 2018;52(1): 27-37
 Bokhust LP et al, Eur Urol 2014; 65: 329-36
 Alpert PF, Urology 2018; 118: 119-26

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A few important facts...

- Early measurement of PSA in a man's 40's can predict lifetime risk of dying from PCa.
 - Low risk men with consistently low PSAs (<1ng/ml) can stop screening in their 60's
 - ↪ Subsequent risk of death is only 0.2%

Vickers AJ et al, BMJ 2010; 341: C4521

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What has fuelled progress?



Medical factors?

Government / NHS initiatives?

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Can we improve PSA?

- Prof. Paula Mendes
 - Professor of Nanotechnology, Birmingham
- Identified 50 forms of PSA
 - All with the same protein
 - But with different sugars attached
 - ↪ Sugars linked to different problems with the prostate – including cancer
 - ↪ Only 4 forms of PSA are associated with PCa

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What has fuelled progress?



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Can we improve PSA?

- Current PSA test involves all of the 50 forms of PSA
 - Relies on detecting the protein involved and not the sugars
- New PSA test hopes to identify each type of sugar using coloured nanoparticles
 - The more sugars that are detected the greater the chance of having an aggressive PCa

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Better than any Government initiative?



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What has upset me the most over past 11 years?

- Is the sound bite now more influential than reading the whole story?
- Can lead to mis-information



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Misleading sound bites

“PSA tests should not be offered routinely to men without symptoms of prostate cancer”

Royal College of GPs , March 2018

Has lead to a large number of men being refused a PSA test by their GP – despite being in a known high-risk category

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Misleading sound bites

“10 year mortality from PCa is unaffected by treatment”

On the face of it true BUT.....

- Progression of disease worse if untreated
- Many men → treatment before 10 years
- QOL issues worse
- Side effects worse in Rx group (but also occurred in non-treatment group)
- PSA tested **ONLY ONCE** (no serial testing)

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Misleading sound bites

“PSA tests should not be offered routinely to men without symptoms of prostate cancer”

Royal College of GPs , March 2018

- Most men with early PCa have no symptoms
- Only 45% men have early PCa at time of diagnosis
- 17% men have metastatic disease at time of diagnosis
- Localised disease has better treatment outcome

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Misleading sound bites

“10 year mortality from PCa is unaffected by treatment”

On the face of it true BUT.....

Studies using serial monitoring of PSA have shown a reduction in mortality

- Progression of disease worse if untreated
- Many men → treatment before 10 years
- QOL issues worse
- Side effects worse in Rx group (but also occurred in non-treatment group)
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Misleading sound bites

“PSA tests should not be offered routinely to men without symptoms of prostate cancer”

Royal College of GPs , March 2018

- Has this been one of the most negative influences on PCa in the past 5 years?



Personal opinion

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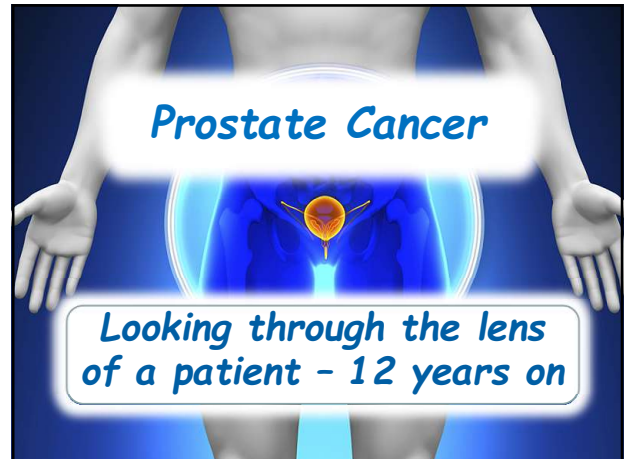
Misleading sound bites

“Prostate cancer now kills more people than breast cancer”

Guardian headline – Feb 2018

- True – but it’s because more men are being diagnosed
- Overall, the % death rate is falling
- The incidence of over-treatment of PCa is at its lowest level ever

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The Future



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Any questions?



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