Public Health England

Protecting and improving the nation's health

Developments and justification of applications using ionising radiation in the medical field

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MERIT, Public Health England

Nordic Society for Radiation Protection - 26 August 2015, Roskilde, Denmark

System of Protection - ICRP

Principles :-

Justification – more good than harm

Optimisation - ALARA

Dose limitation – applies to planned exposures only

Exposure situations :-

planned exposures, existing exposures, emergency exposures

Categories of exposure :-

occupational

public

medical

NB medical exposures are planned but not subject to dose limitation

Protection in Medical Exposures

Compensate for lack of dose limitation by ;-

diagnostic reference levels, [dose constraints]

additional level of justification

ICRP specifies 3 levels of justification

Level I – use of radiation in medicine

Level II – types or classes of practice

Level III – individual patient level

Justification in Medical Exposures

European Basic Safety Standards Directive 2013/59/Euratom

Justification Level III

Article 55 – benefit outweighs detriment

Justification Level II

Article 19.1 – types or classes justified before being adopted

Article 19.2 – review existing types or classes if new evidence

Article 19.4 – consider occupational and public exposure

Level II Justification in Medical Exposures

Article 19.1

Member States shall ensure that new classes or types of practices…… are justified before being adopted

What is a type or class of medical exposure?

What are the options for competent authorities?

What are the practical implications?

Level II Justification in Medical Exposures

What are the options for competent authorities?

Generic v specific approach

What are the practical implications?

Realistic mechanisms in the face of rapid technological change

Level II Justification in Medical Exposures

Factors or data to consider

CE marking

Marketing Authorisation

Availability

Professional guidance, best and established practice and peer reviewed research

Level II Justification in Medical Exposures

Generic Approach

identify key descriptors

- modalities under consideration
- types of medical exposure

eg. use of radiography for health screening programmes

national breast cancer screening programme - YES

eg. use of CT for health screening programmes

national lung cancer screening programme - NO

Level II Justification in Medical Exposures

Advantages (for regulators)

simple to understand

simple to update

approach applicable and consistent across sectors

Disadvantages (for users)

difficult to understand

seems to only apply to major changes

NB provides limited control of day to day medical practice

Level II Justification in Medical Exposures

Specific Approach

identify detailed descriptors

- modality under consideration
- specific procedure/investigation under consideration
- specific condition under consideration
- specify role in clinical pathway

eg. use of PET CT using 18F fluoro - choline in diagnosis for prostate cancer - YES

eg. use of PET CT using 18F fluoro - choline in diagnosis for bladder cancer - NO

Level II Justification in Medical Exposures

Advantages (**for users)**

simple to understand

applies to day to day practice

Disadvantages (**for regulators)**

complexity means difficult/impossible to provide timely updates

neither applicable nor consistent across sectors

NB provides detailed control of day to day medical practice

Examples of New Types or Classes of Medical Exposures

Introduction of a new application of existing equipment based type or class of medical exposure

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Introduction of a new drug based type or class of medical exposure

molecular radiotherapy using alpha emitters

Case Study One

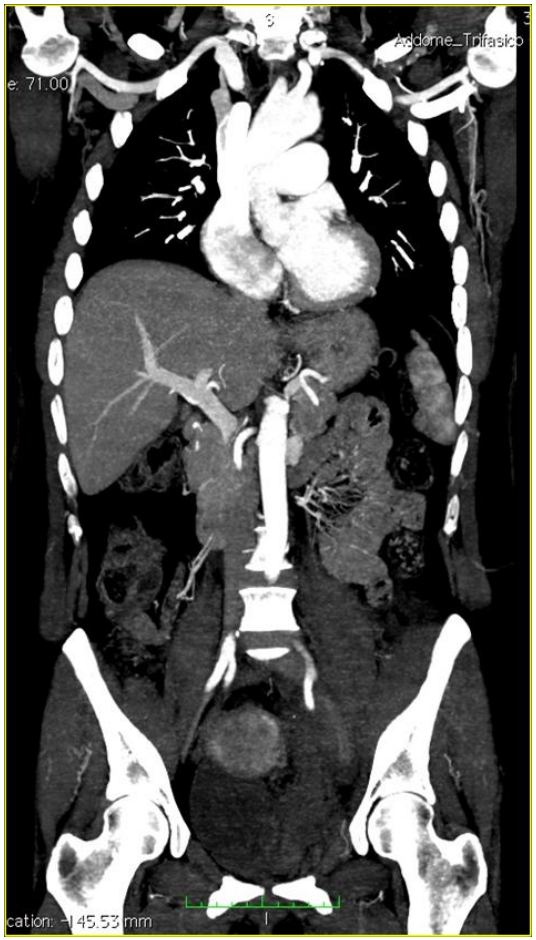
Introduction of a new application of existing equipment based type or class of medical exposure

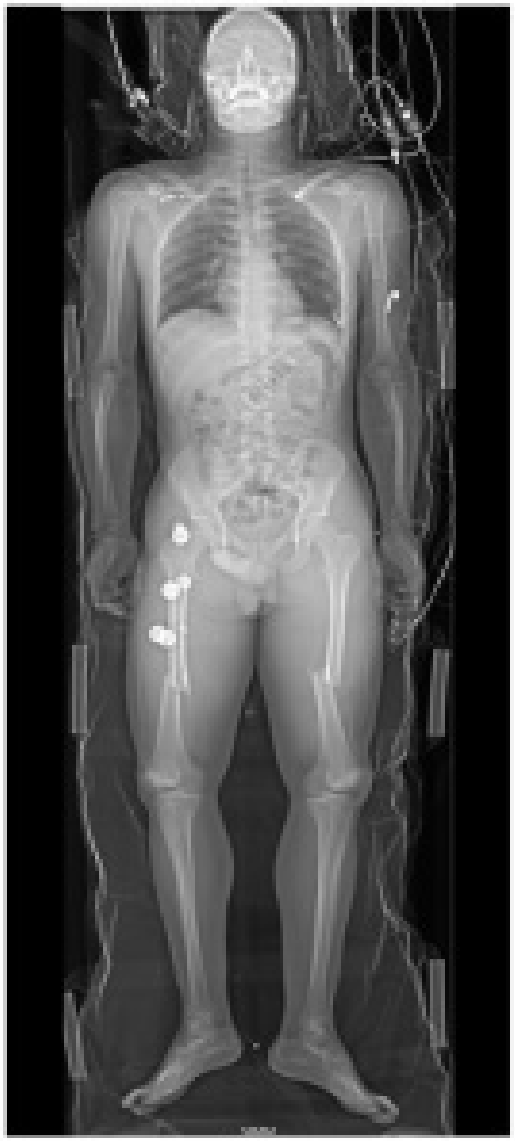
Whole body scanning for Individual Health Assessment using Computed Tomography (CT)

“Offers early detection of significant conditions, thus enhancing potential treatment success”

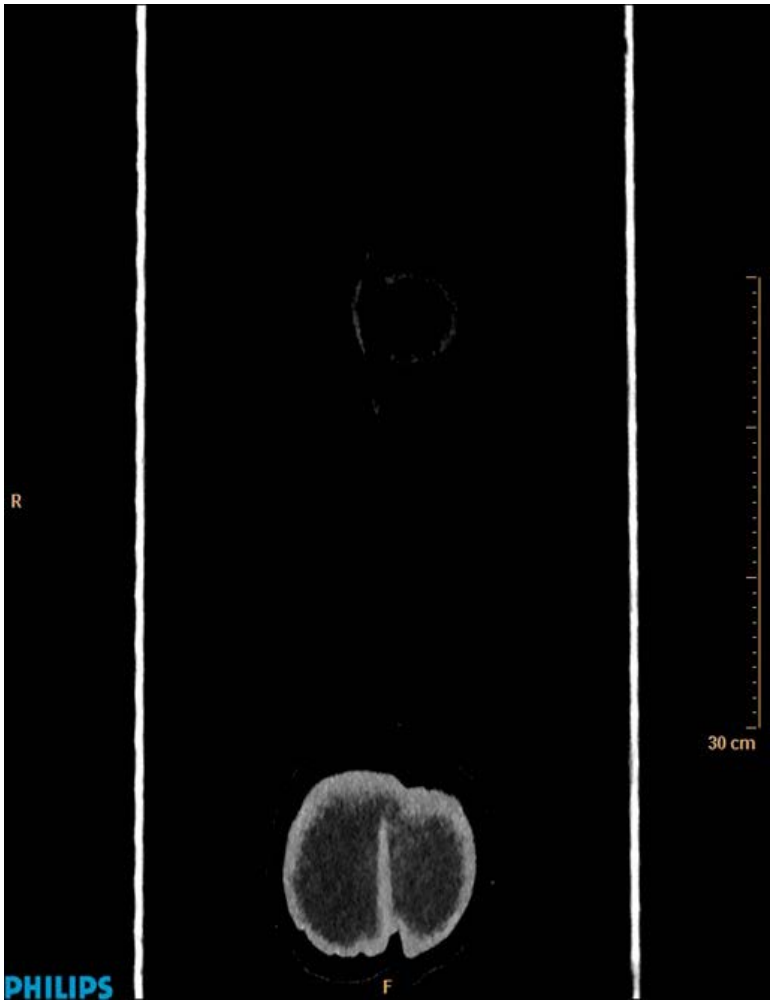
Whole Body Imaging – Diagnosis

Single scan using dual phase contrast injection demonstrates arterial and portal venous phases on one scan





Whole Body Imaging



Whole Body Imaging – Individual Health Assessment

Established technology - CE marked equipment

Established investigation – whole body imaging using CT

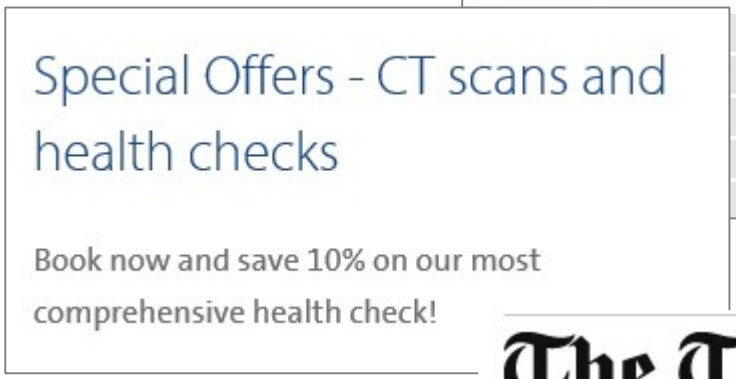
Established conditions

- lung cancer, coronary heart disease, colorectal cancer
- spinal problems, osteoporosis, body fat assessment

But is it diagnosis/early diagnosis?

……. symptoms or risk?

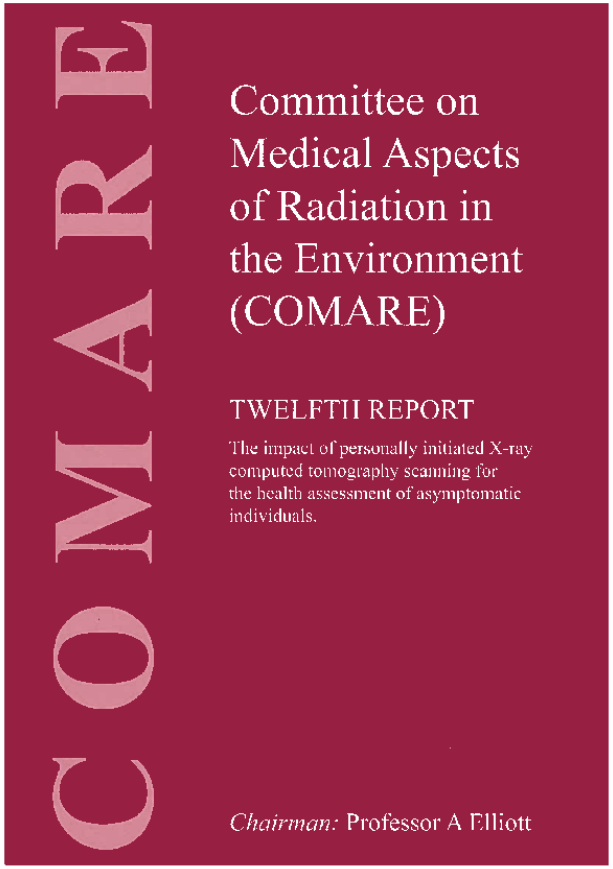
Whole Body Imaging of the 'Worried well' - (IHA)



Whole Body Imaging of the 'Worried-well'

Response to COMARE recommendation:

> "The evidence on the justification of x-ray exposures drawn from the COMARE report and from the consultation confirm that whole-body (neck to pubic symphysis), non-targeted, spinal, osteoporosis and body fat IHA CT scans are very unlikely to be justified."



Changes to Legislation

Regulation 3:

These Regulations shall apply to the following medical exposures –

a) The exposure of patients as part of their own medical diagnosis or treatment, including any exposure of an asymptomatic individual

b) The exposure of individuals as part of occupational health surveillance

c) The exposure of individuals as part of health screening programmes

d) The exposure of patients or other persons voluntarily participating in medical or biomedical, diagnostic or therapeutic, research programmes

e) The exposure of individuals as part of medico-legal procedures

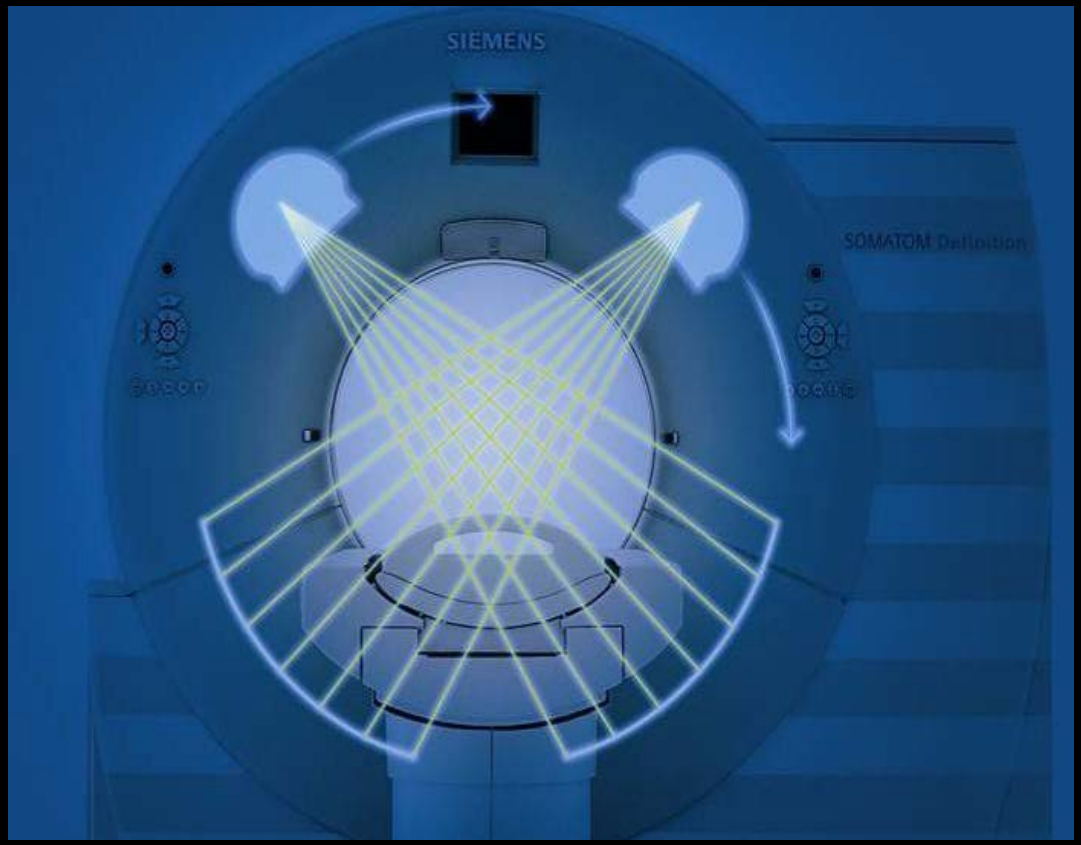
Case Study Two

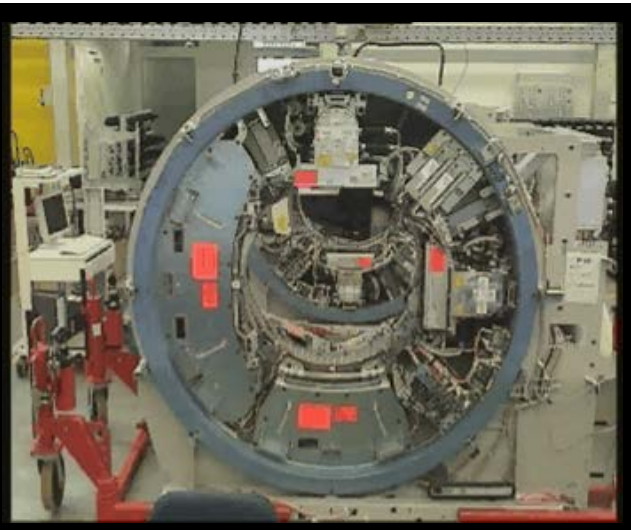
Introduction of a new equipment based type or class of medical exposure

Diagnosis using dual energy Computed Tomography (CT)

“Offers different attenuation levels between materials enabling more detailed classification of pathology”

Dual Source CT – 2 X-Ray Tubes and 2 Detectors





SOMATOM Force – The All New Dual Source CT

New key components

Vectron tube

0.4 x 0.6 mm focal spot, 1,300 mA @ 70, 80, 90 kV

Stellar Infinity detector

2 x 96 rows (2 x 6 cm)

1.840 channels

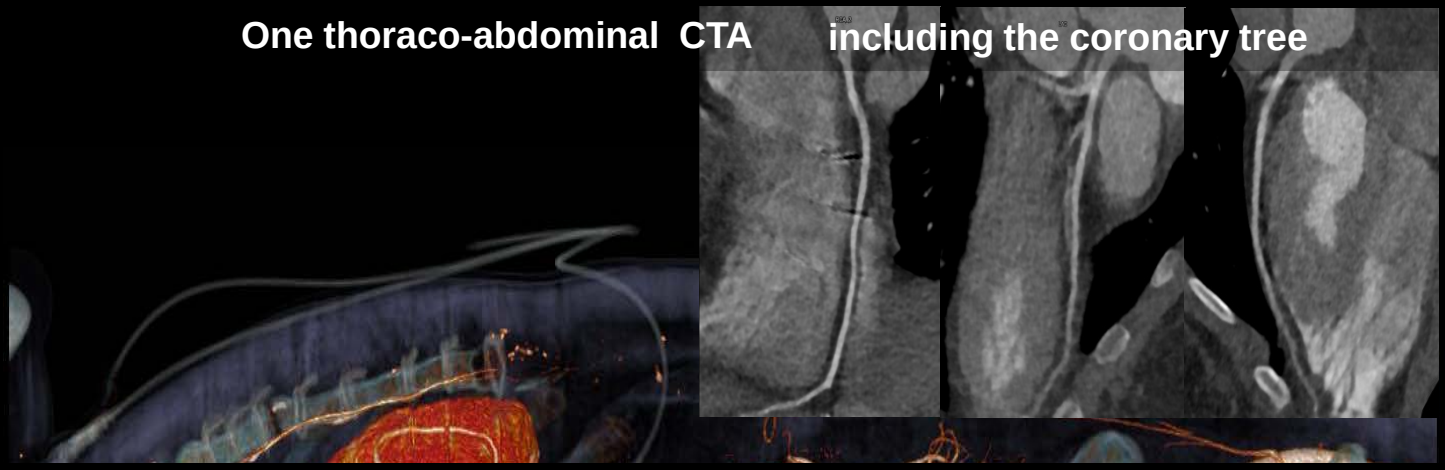
Contactless data/power transmission

2 x 8.5 Gbit/s

High-speed patient table

737 mm/s speed

Triple-rule-out Turbo Flash scan with no breath hold in acute chest pain – kidney friendly



60% of Aortic Dissections are Type I, requiring long scan ranges

SOMATOM Force

collimation: 192 x 0.6 mm
scan time: 0.80 s
scan length: 591 mm
rotation time: 0.25 s
90 kV, 398 mAs
CTDIvol: 2.8 mGy
DLP: 177 mGycm
2,6 mSv
HR: ~ 73 bpm

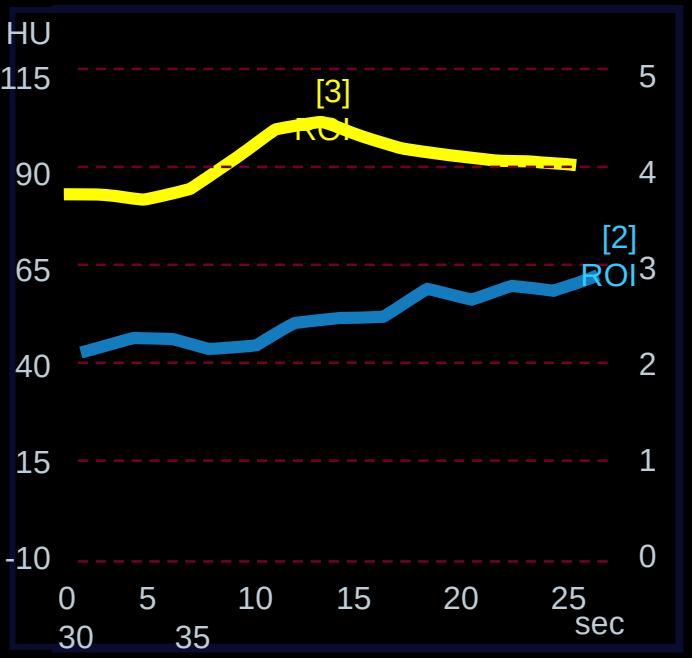
Turbo Flash scan reveals root cause of atypical chest pain - a DeBakey Type I aortic dissection

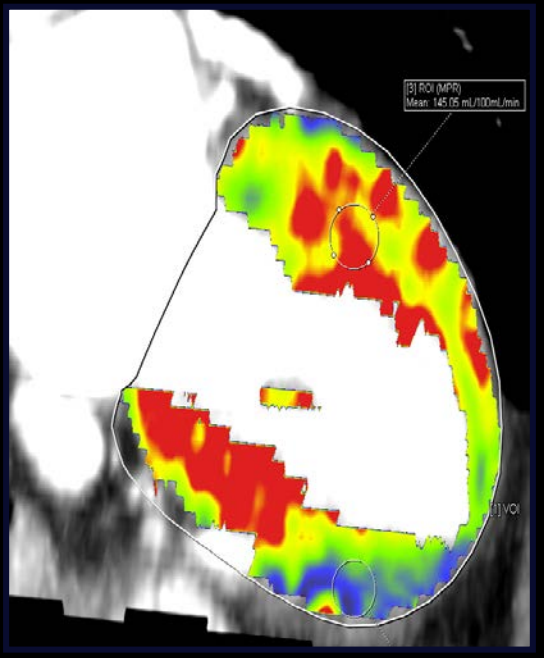
Radiologie LMU Grosshadern / Munich, Germany

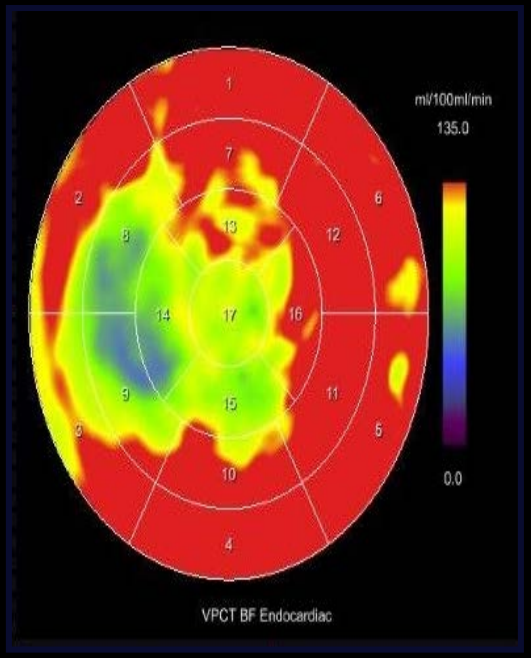
Dynamic myocardial stress perfusion - combining diagnostic and functional imaging at low dose

End-systolic ECG triggering for a thick myocardium, without beta-blockade and under adenosine stress.

80 kV, 117 mAs, 4.4 mSv







Courtesy of Erasmus MC, Rotterdam

Lung imaging - high accuracy for nodule detection even at the dose of conventional X-ray[1]

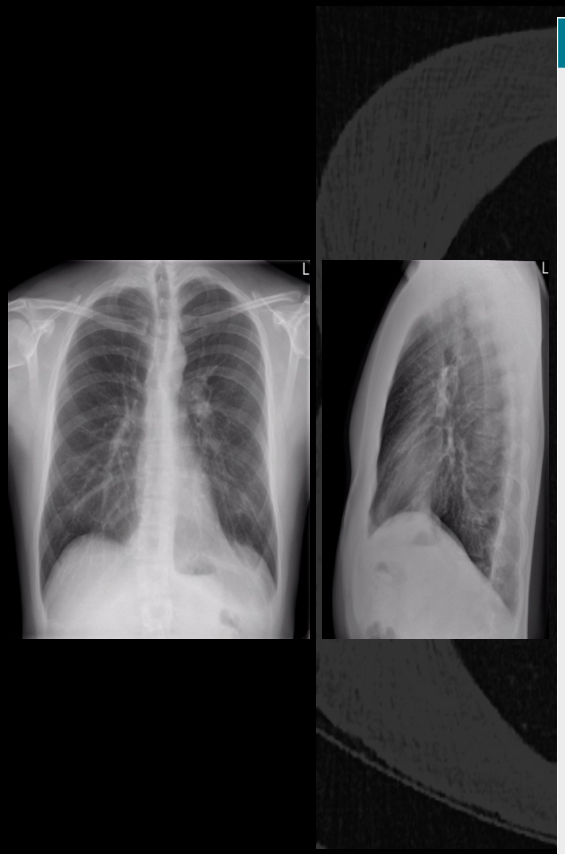


Table 1 Radiology 2008;248:254-63

Adult Effective Doses for Various Diagnostic Radiology Procedures

Examination	Average Effective Dose (mSv)	Values Reported in Literature (mSv)
Skull	0.1	0.03–0.22
Cervical spine	0.2	0.07–0.3
Thoracic spine	1.0	0.6–1.4
Lumbar spine	1.5	0.5–1.8
Posteroanterior and lateral study of chest	0.1	0.05–0.24
Posteroanterior study of chest	0.02	0.007–0.050
Mammography	0.4	0.10–0.60
Abdomen	0.7	0.04–1.1
Pelvis	0.6	0.2–1.2
Hip	0.7	0.18–2.71
Shoulder	0.01	. . .
Knee	0.005	. . .
Other extremities	0.001	0.0002–0.1
Dual x-ray absorptiometry (without CT)	0.001	0.001–0.035
Dual x-ray absorptiometry (with CT)	0.04	0.003–0.06
Intravenous urography	3	0.7–3.7
Upper gastrointestinal series	6*	1.5–12
Small-bowel series	5	3.0–7.8
Barium enema	8*	2.0–18.0
Endoscopic retrograde cholangiopancreatography	4.0	. . .

SOMATOM Force

Dual Selective Photon Shield

collimation: 2x 192 x 0.6 mm

rotation time: 0.25 s

tube setting: 100 kV Sn

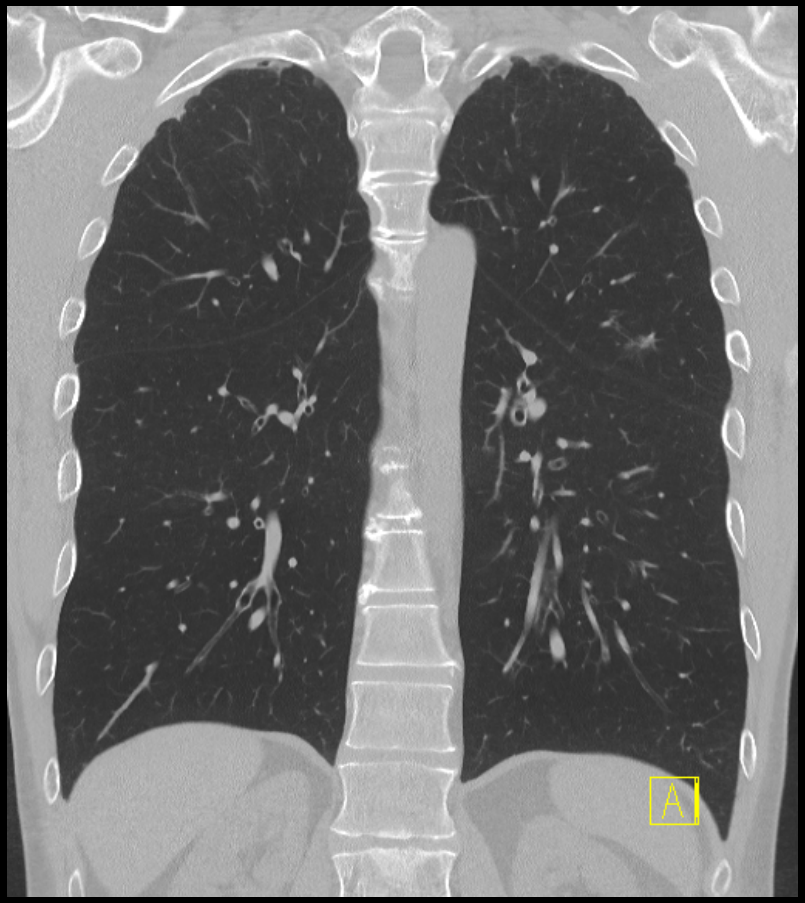
0.06 mSv

Lung examinations with significantly improved air-to-soft-tissue contrast allow doses of conventional X-ray[1]

Courtesy of University Hospital of Zürich, Switzerland

1) Invest Radiol. 2014 Jul;49(7):465-73.

Low dose early detection lung cancer - low dose lung CT at enhanced soft-tissue-to-air contrast



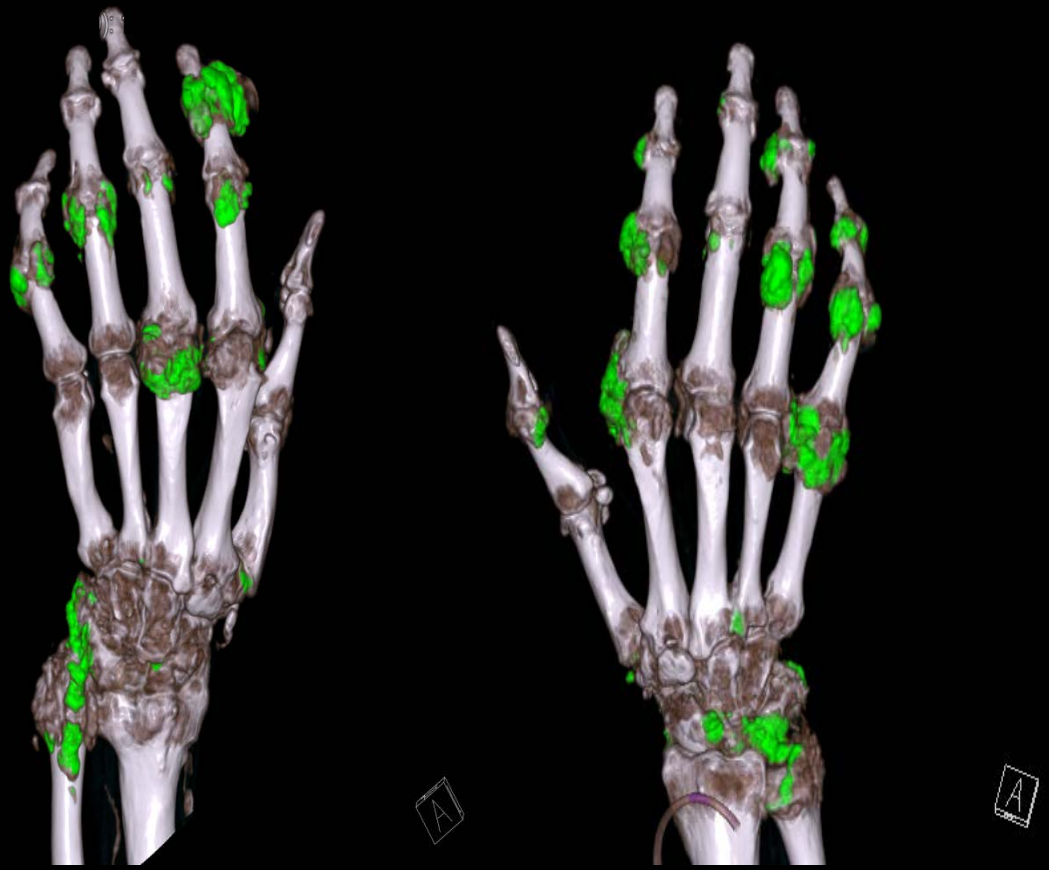
SOMATOM Force

Dual Selective Photon Shield
collimation: 192 x 0.6 mm
rotation time: 0.25 s
tube setting:
100 kV Sn
0.1 mSv

Significantly improved air-to-soft-tissue contrast due to 100 kV Sn scan mode (Dual Selective Photon Shield II)

Courtesy of UMM, Mannheim, Germany

Gout diagnosis and evaluation with Dual Energy CT



TwinBeam Dual Energy

collimation: 64 x 0.6 mm

scan time: 8 s

scan length: 218 mm

rotation time: 0.5 s

tube setting: AuSn120 kV, 298 eff. mAs

CTDIvol: 6.4 mGy

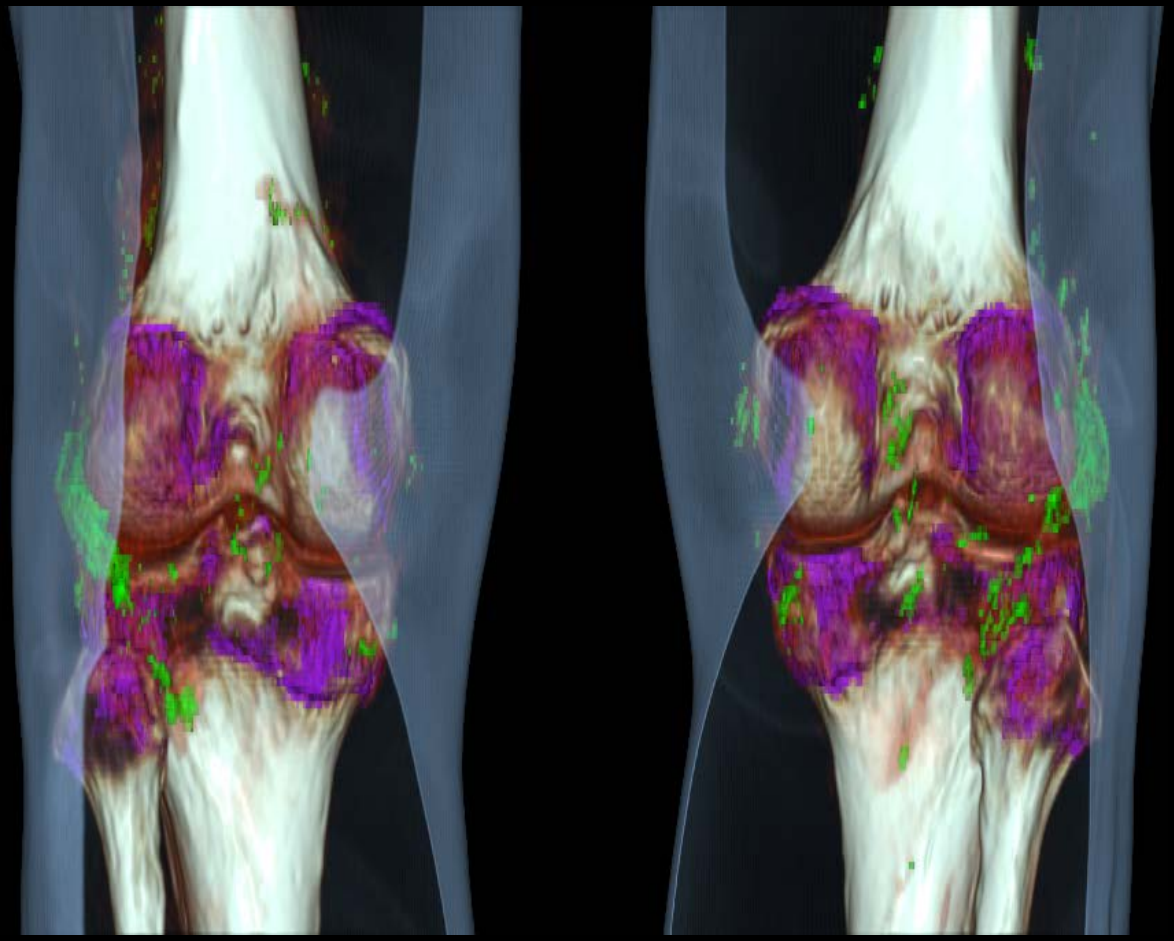
DLP: 141 mGycm

Eff. Dose: 0.11 mSv

Courtesy of Luzerner Kantonsspital, Luzern, Switzerland

*TwinBeam Dual Energy is pending 510(k) clearance and is not yet commercially available in the United States
Post processing software is under development. Not available for sale in the U.S.

Accurate and non-invasive diagnosis of gout



SOMATOM
Definition
AS+

80/140 kV
eff. dose: 0.13 mSv

Single Source
Dual Energy

Courtesy of Nan Xi Shan Hospital / Guilin, China

Diagnosis using Dual Energy CT

Established technology - CE marked equipment

Established technique –diagnostic imaging using CT

Established benefits for patients with underlying conditions (eg contrast reduction)

- aortic dissections, coronary heart disease, lung cancer

- gout

Is diagnosis really necessary for all using CT?

Case Study Three

Introduction of a new drug based type or class of medical exposure

Molecular radiotherapy using alpha emitters

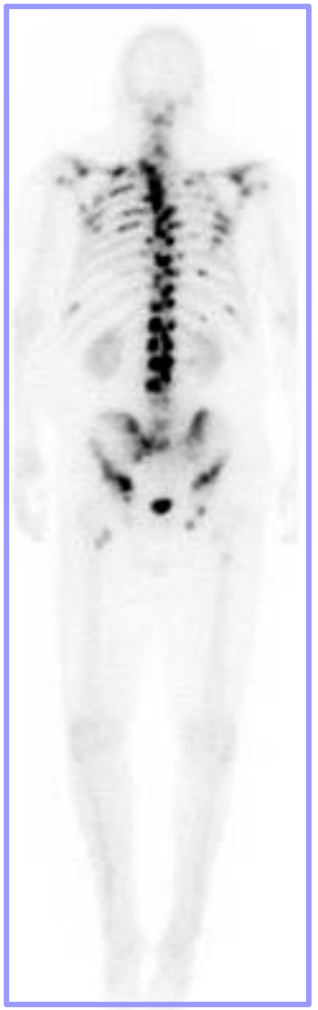
“Offers effective palliation for patients with bone metastases with reduced myelosuppression”

Skeletal metastases

> 90% of metastatic patients [1]

↑ surgery / EBRT for skeletal-related events [2]

↑ disability, QOL impairment, treatment cost & death [3]



1. Tannock et al. N Engl J Med. 2004;351:1502-1512.
2. Lipton. Semin Oncol. 2010;37:S15-S29.
3. Lange and Vasella. Cancer Metastasis Rev. 1999;17:331-336.

Molecular Radiotherapy

Bone seeking radiopharmaceuticals

- **^{32}P orthophosphate**
- **$^{89}SrCl_2$**
- **^{153}Sm EDTMP**
- **^{186}Re HEDP**
- **^{188}Re HEDP**

β^- particle emitting radiolabels

Effective palliation but

- **myelosuppressive**
- **no survival benefit**

→ **declining use**

EDTMP, ethylenediamine tetra(methylene phosphonic acid); HEDP, hydroxyethylidene diphosphonate; ^{32}P, phosphorous-32; ^{186}Re, rhenium-186; ^{188}Re, rhenium-188; ^{153}Sm, samarium-153; $^{89}SrCl_2$, strontium-89 dichloride

Radium: Physical Properties

Ca^{2+} analogue

Radium 223 (^{223}Ra)

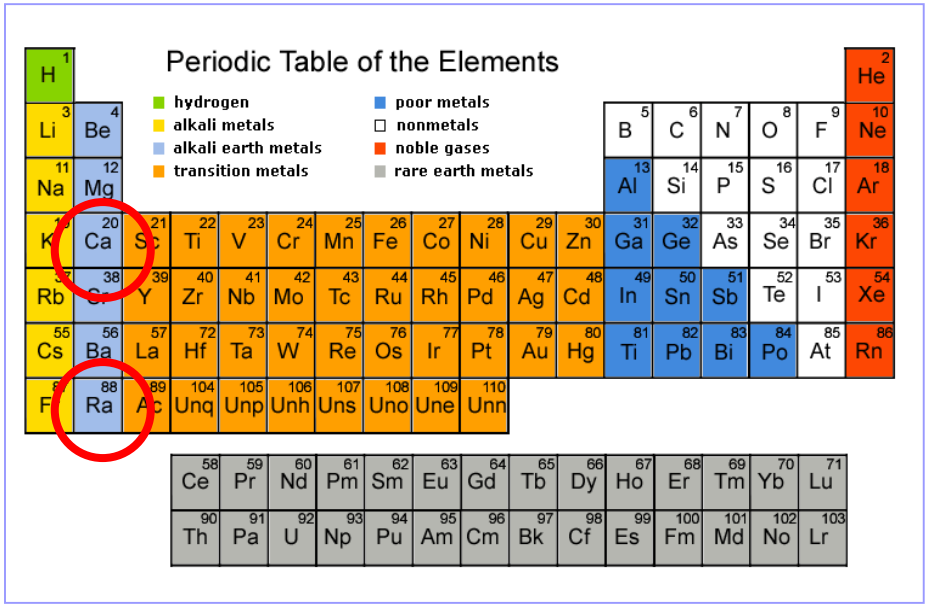
$t_{1/2}$ = 11.4 days

95.5% alpha

3.6% beta

1.1% gamma

28.2MeV decay energy

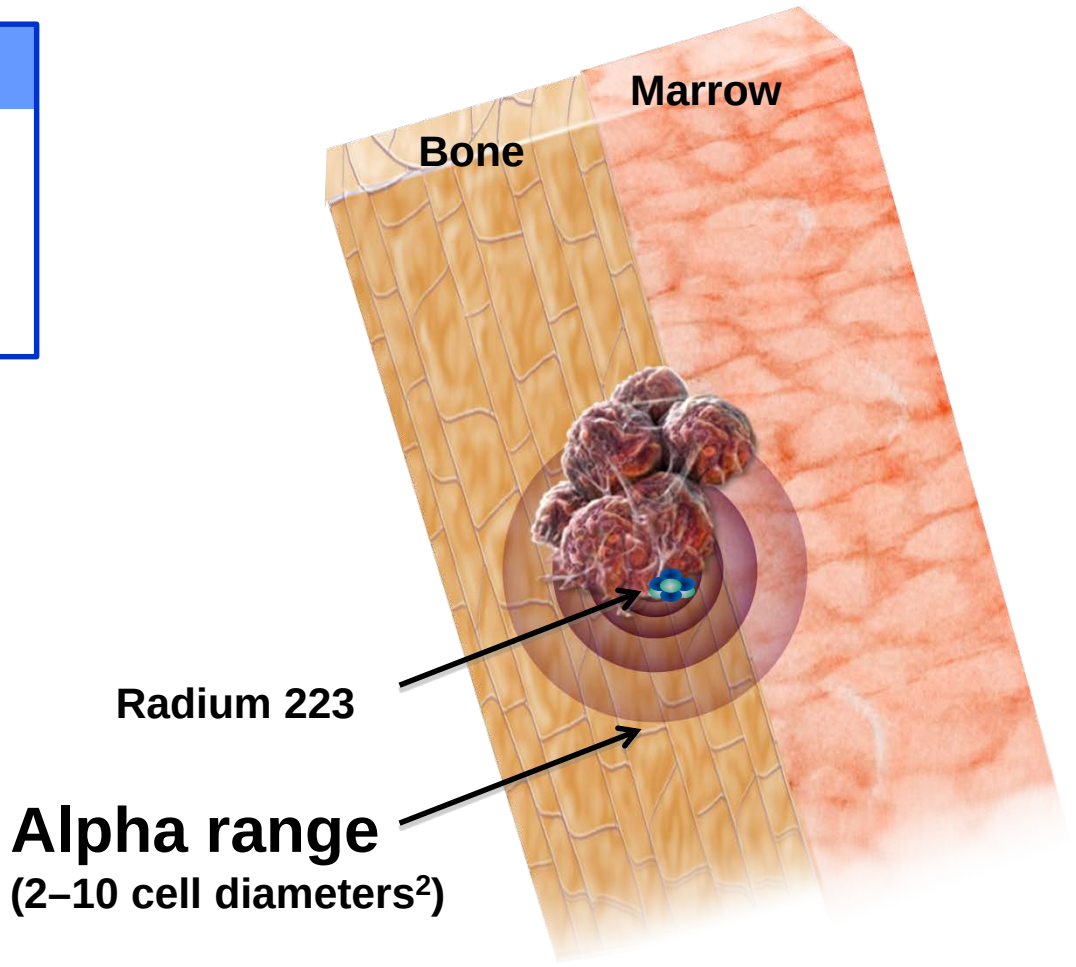


Adapted from Henriksen et al. Cancer Res 2002;62:3120–5.

Nuclides 2000, Nuclide Explorer, Institute of Transuranium Elements Karlsruhe, Germany (1999) Version 1.0

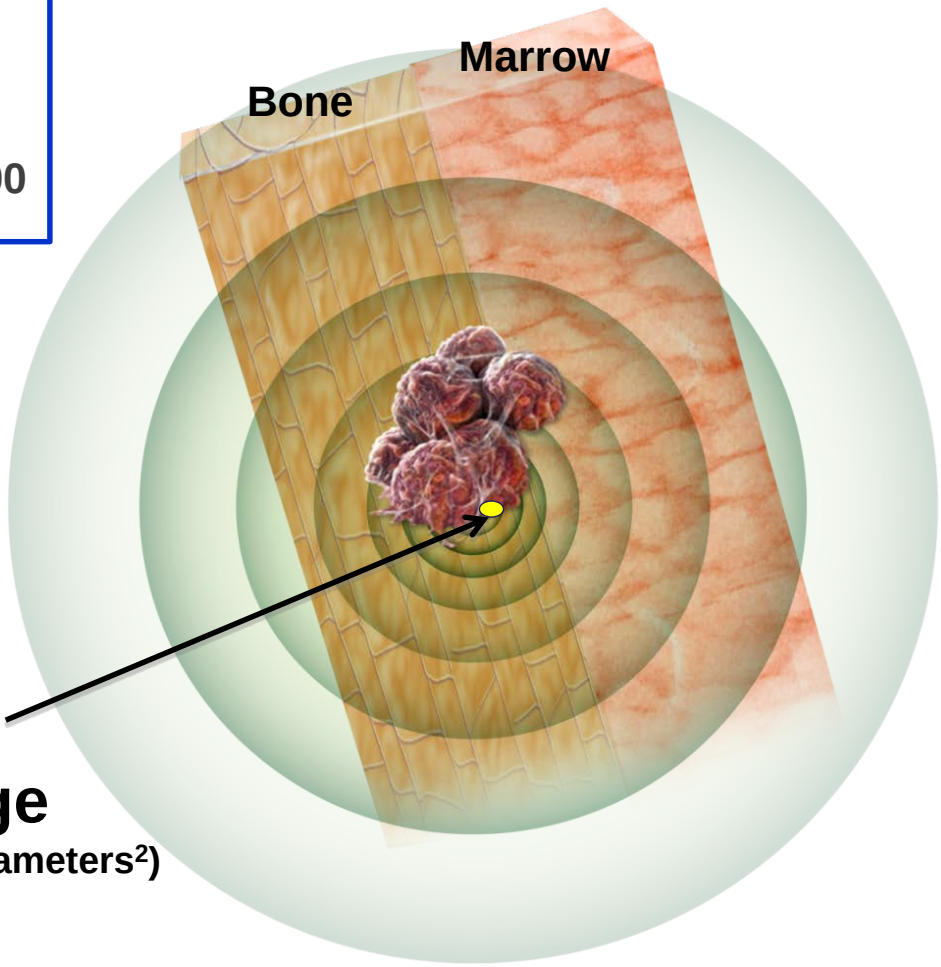
Particle Range

	Alpha
Relative particle mass	7000
Range in tissue (μm)	40–100



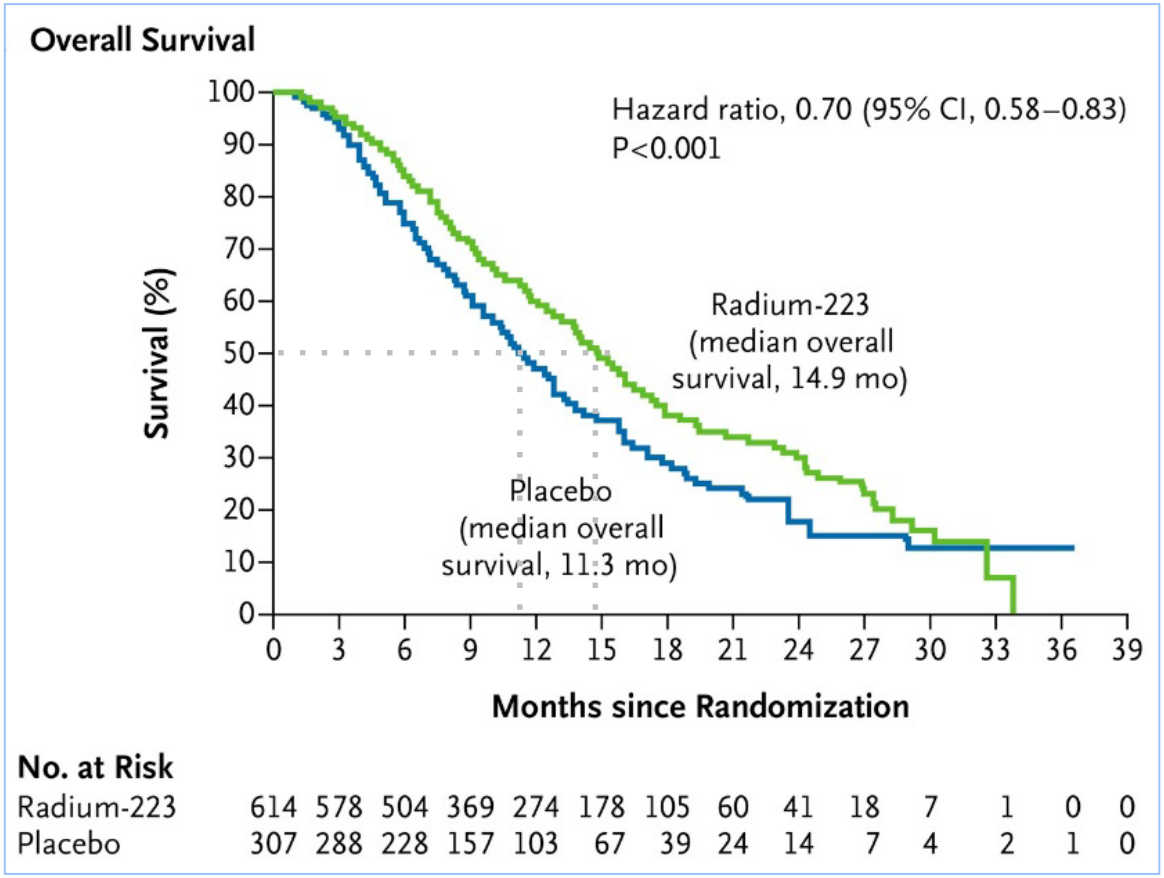
Particle Range

	Alpha	Beta
Relative particle mass	7000	1
Range in tissue (μm)	40–100	50–12 000



ALSYMPCA Overall Survival

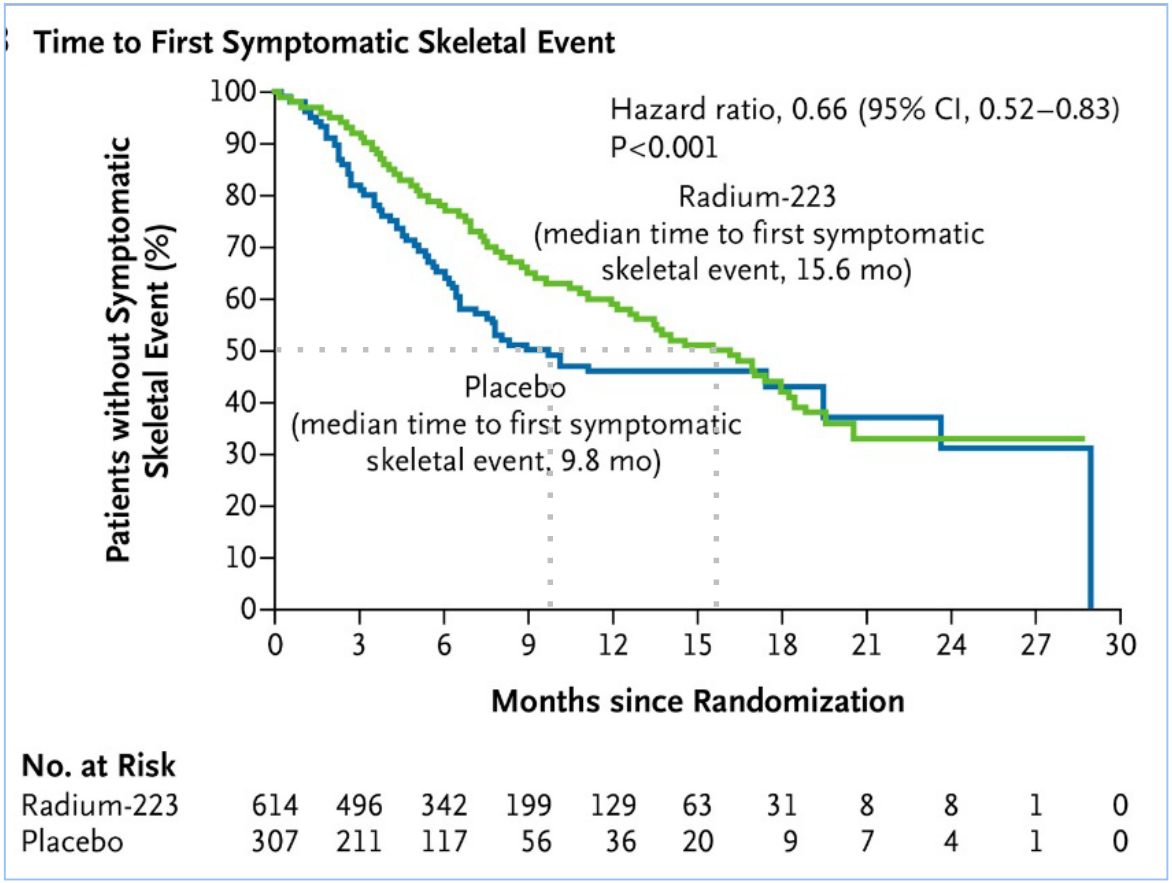
ALpharadin in SYMptomatic Prostate CAncer



3.6m median OS gain (11.3 v 14.9 m)

Parker C et al. N Engl J Med 2013;369:213-23

ALSYMPCA Symptomatic Skeletal Event



1st SSE delayed by 5.8 m (15.6 v 9.8 m)

Parker C et al. N Engl J Med 2013;369:213-23

Expanded Access Programme (US)

- Phase 2 prospective, interventional, open-label, multicenter United States EAP Study (15995)
- Cancer resistant prostate cancer patients with symptomatic bone metastases (mCRPC)
- Acute and long-term safety evaluated

RESULTS

- 253 patients enrolled
- 184 patients received ≥1 Ra-223 injection
- Median number of injections EAP = 5 vs ALSYMPCA = 6

Vozelzang NJ et al. J Clin Oncol 33,2015
(Suppl 7; Abstr 247)

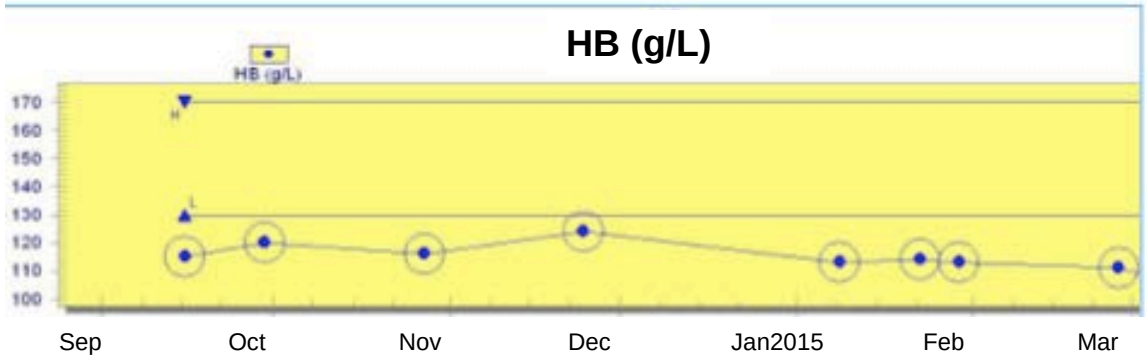
Radium-223: US Expanded Access Programme

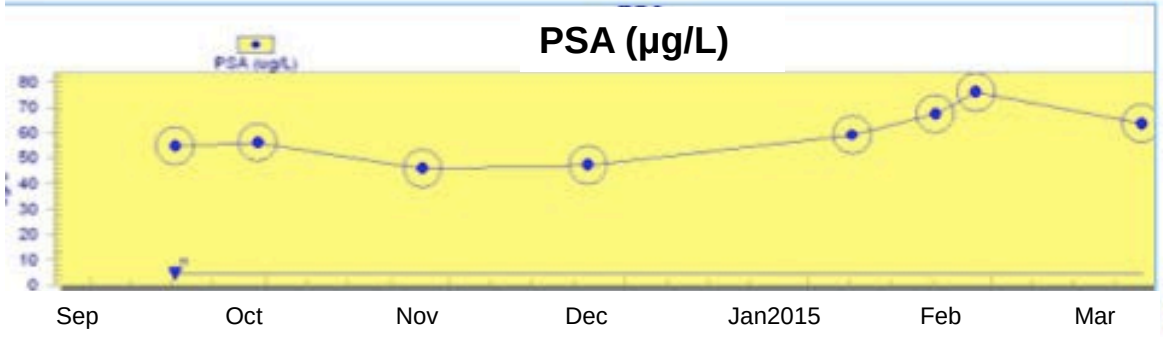
In heavily pretreated patients with CRPC and symptomatic bone metastases, US EAP results confirm

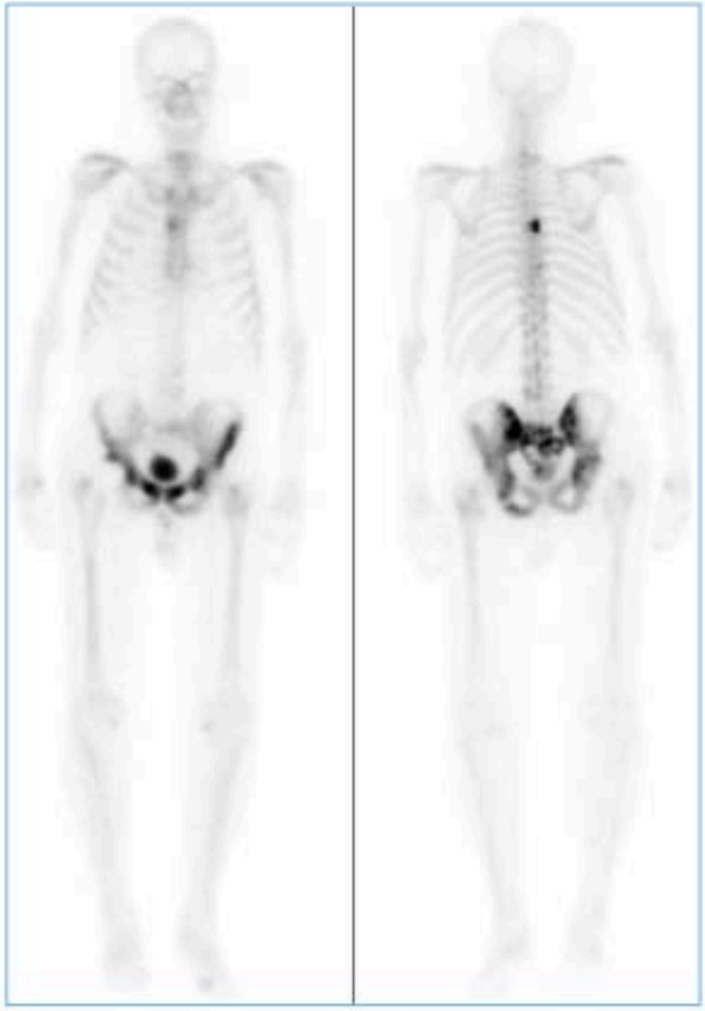
- **Ra-223 is well tolerated**
- **No secondary malignancies attributable to Ra-223**
- **Increased median OS benefit compared with ALSYMPCA population**

Vozelzang NJ et al. J Clin Oncol 33,2015 (Suppl 7; Abstr 247)

Patient Selection

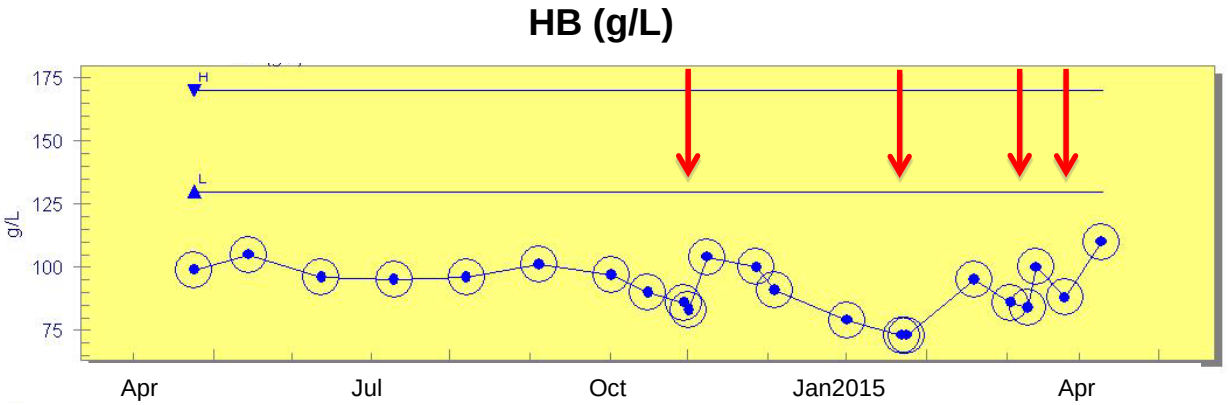


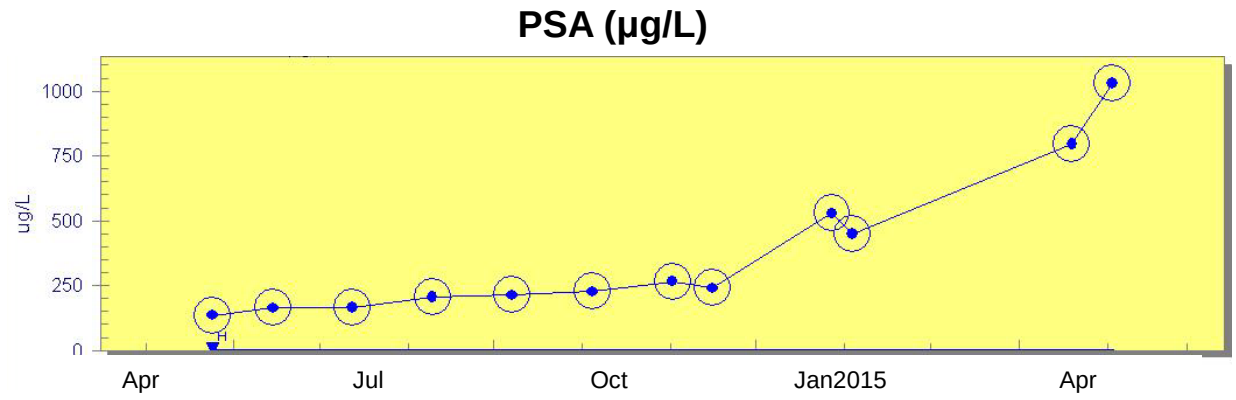


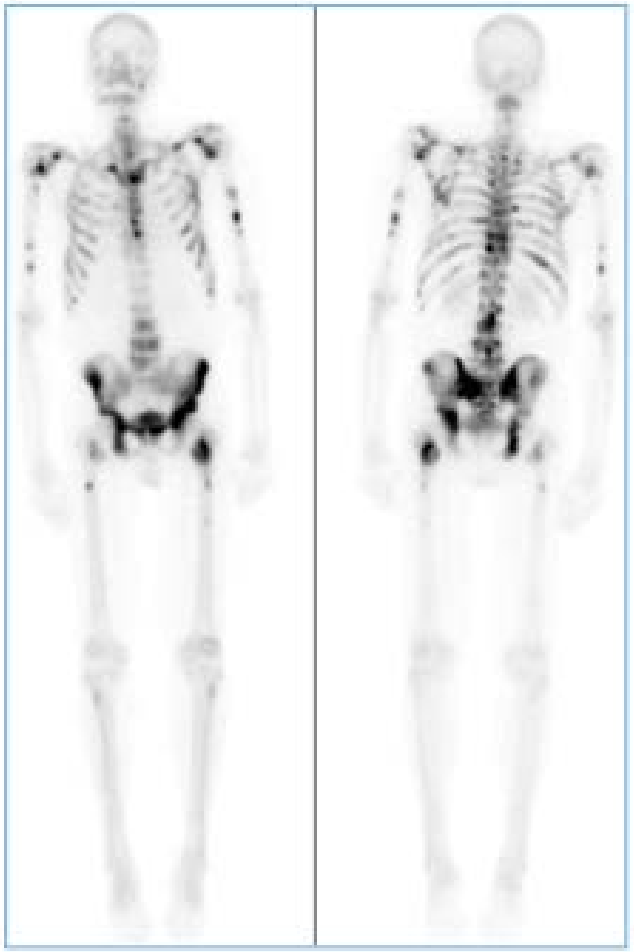


HB, haemoglobin
PSA, prostate-specific antigen

Patient Selection

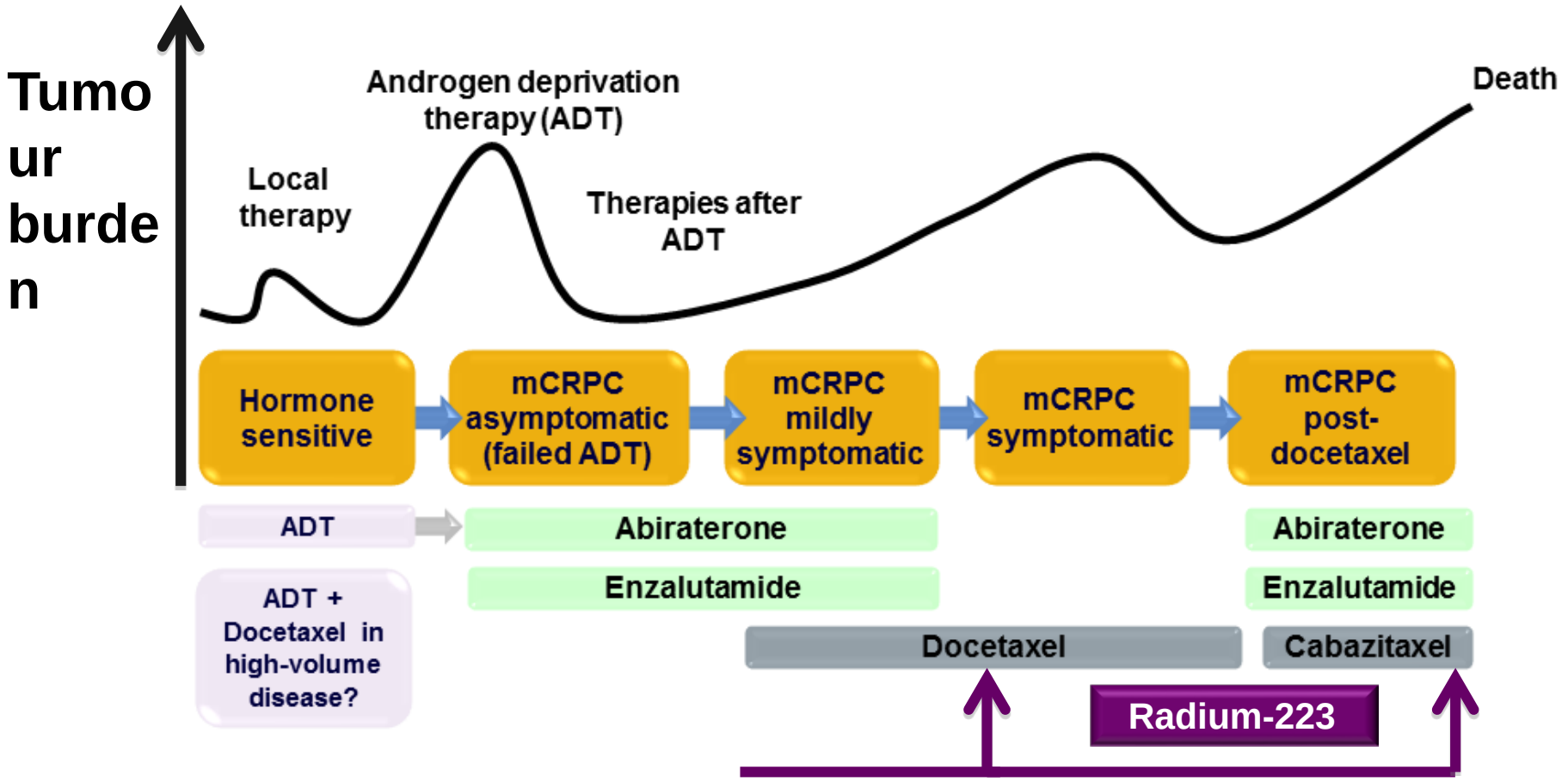






HB, haemoglobin
PSA, prostate-specific antigen

Nuclear medicine and mCRPC 2015



Summary

Radium-223 in mCRPC

Radium-223 (50 $kBqkg^{-1}$ x 6)

- **Significantly improves median OS by 3.6 m**
- **Delays median time to first SSE by 5.5 m**
- **Well tolerated**

- **EU Expanded Access Programme results awaited**
- **Further RCTs required**

Molecular Radiotherapy using Alpha Emitters

Established technique (but using beta emitters)

Supportive evidence base from significant trials

Common condition

New application point in clinical pathway

Specific to disease progression

Limited value – OS and SSE (value judgement)

Expensive

Conclusions

Medical technology and its applications develop rapidly

the application of novel techniques to the individual should not be confused with adoption of a type or class of practice

established indicators of routine application (eg CE marking) may not be sufficient on their own – ***hybrid systems*** may be necessary

the boundary between research and accepted practice is blurred and the level of evidence applied to imaging and therapy medical applications may be different

Conclusions

Justification at Level II for new types or classes of practice for medical exposures is not simple

To what degree should Competent authorities get involved with clinical applications – even at Level II ?

Competent authorities will need processes in place to demonstrate that they are satisfying requirements under BSS Directive 2013/59/Euratom Article 19

Ideally approaches and processes should be consistent and should apply to all new types or classes of practice – AND NOT JUST MEDICAL EXPOSURES

Conclusions

To the audience

– THANK YOU

To Competent authorities

- GOOD LUCK

Acknowledgements

Prof. Val Lewington – Guys and St Thomas' Hospital, London

Miss Sarah Peters – Public Health England

Siemens

Philips