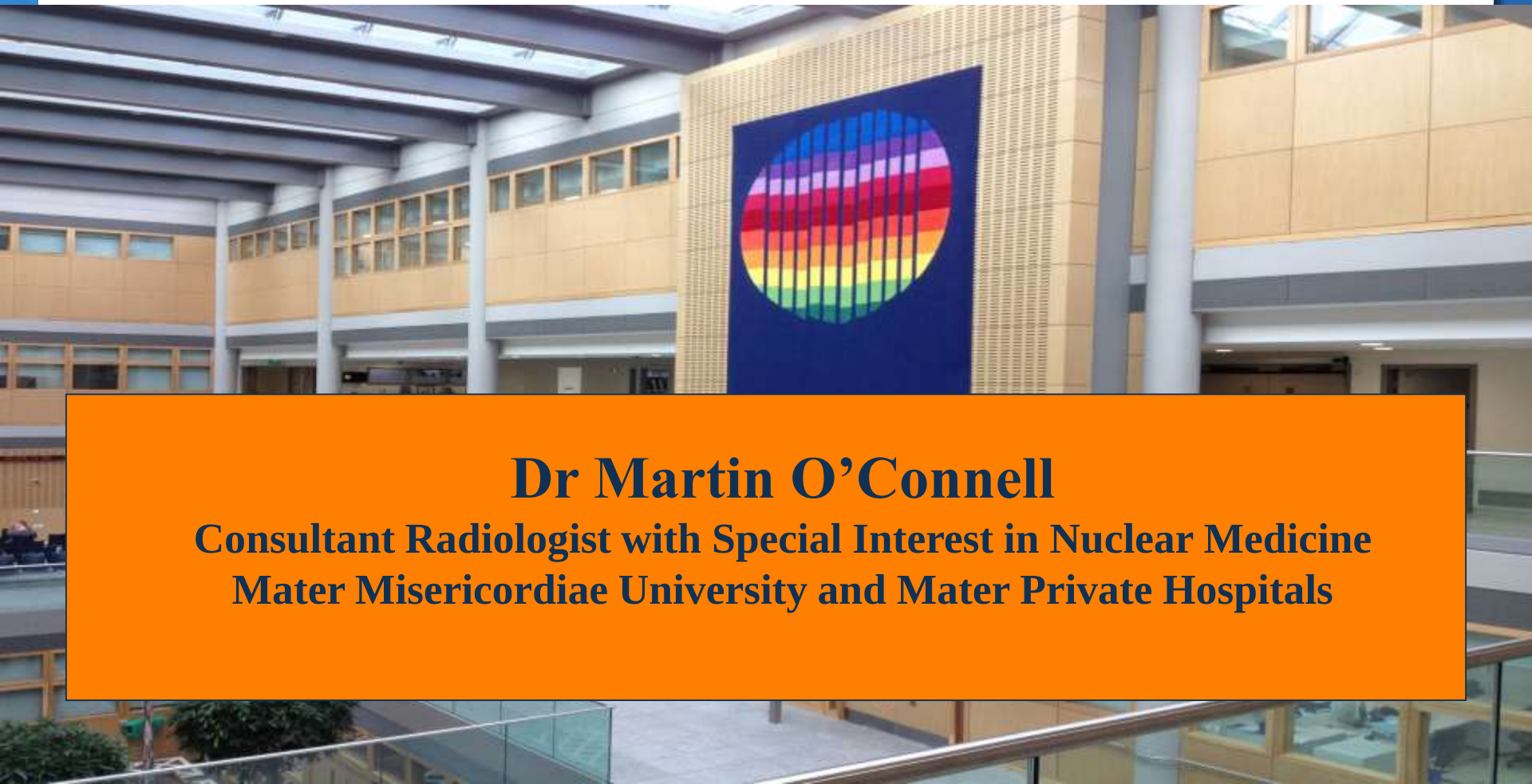
Radiosynovectomy



Dr Martin O'Connell

Consultant Radiologist with Special Interest in Nuclear Medicine
Mater Misericordiae University and Mater Private Hospitals

Radiosynovectomy

also known as

Radiosynoviorthesis

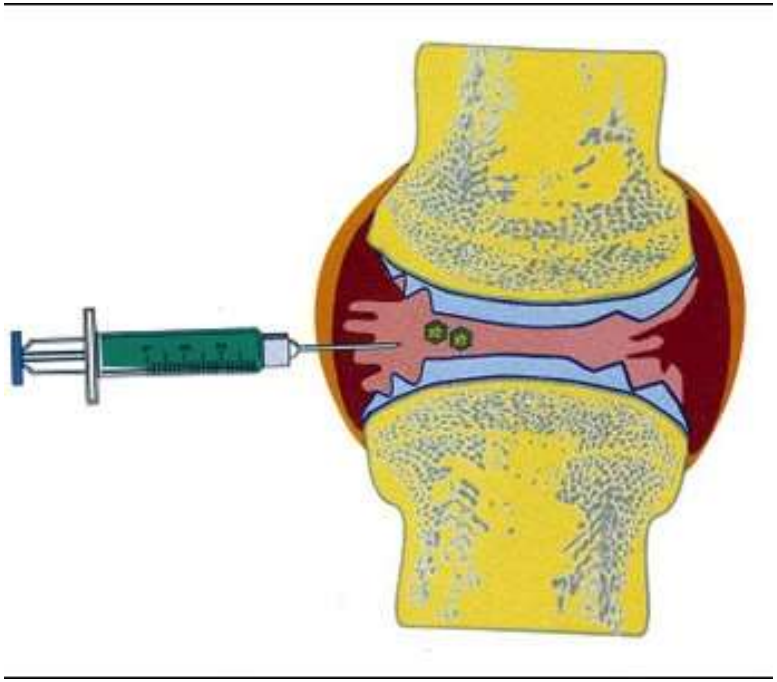
EANM Procedure Guideline 2003

EANM®
European Association of Nuclear Medicine

Principles

- Intra-articular injection of radiocolloid – inflammatory synovitis
- Irradiation of hypertrophic synovial membrane
- Ablation of synovial tissue
- Without damage to underlying articular cartilage

RADIOSYNOVECTOMY (Knee)



- Colloidal isotope phagocytized into synovial cells.

Radiosynovectomy

- Inflammatory Arthritis
- All major joints except spine – Knee is No.1
- Immobilize joint for 48 hours
- Two treatments per joint maximum?
- Up to 4 joints at one sitting?

Failed steroid injection is a pre requisite

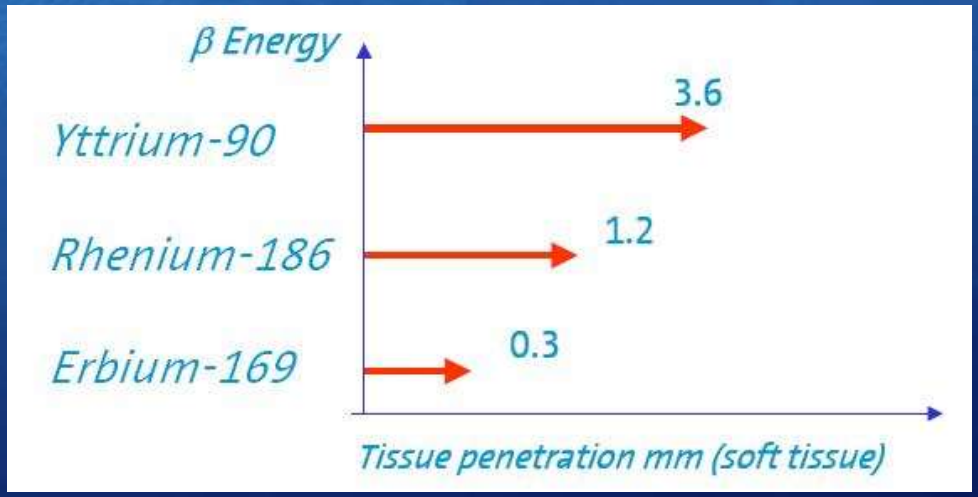
Paradoxically Response to steroid is a pre requisite in some countries

Radiosynovectomy Indications

- Rheumatoid Arthritis
- Seronegative Spondyloarthropathy
- PVNS
- Haemarthrosis in Haemophilia
- Undifferentiated Monoarthritis
- Particle Disease/Polyethylene Disease after joint replacement
- Inflammatory Osteoarthritis (Controversial)

Principles

- Radiation Tissue penetration is proportional to energy of beta particles
- Radionuclide used depends on joint to be treated



Doses
(Colloid particle size 5-10 nm to avoid leakage)

- Y-90 (Large joints – knee)
  - Knees — 185 – 222 MBq in 2-3ml
- Er-169 (Small joints)
  - Finger/Toe joints — 10 – 40 MBq in <1ml
- Re-186 (medium size joints)
  - Shoulder — 70 -110 MBq in 3ml
  - Elbow — 75 MBq in 1 -1.5ml
  - Wrist — 40-75 MBq in 1-1.5ml

Isotopes

- Yttrium – "The sandblaster"

- Rhenium –" A small hammer"

- Erbium- "artist's chisel"

- USA: Dysprosium-165 Iron Hydroxide

Patient assessment and planning

- Failed steroid injection and symptoms for minimum of 6 months.
- Conversely some response to steroids is a marker for potential successful treatment
- Avoid patients with extensive cartilage loss, joint destruction and bone odema – will not help
- No arthroscopic intervention other than Baker's Cyst aspiration in previous 6 weeks
- For knee – 48 hours off work or Inject on Friday
- Choose a "Clean" room for procedure

Patient assessment and planning

- For Knee injection – ultrasound appointment with pre consent and discussion of procedure – Exclude or assess Baker's cyst
- And/or Two phase bone scintigraphy
- And/or MRI – important in PVNS
- Knee injection will require ultrasound
- Other joints need fluoroscopy and contrast with MSK colleague (best operator)
- Confirm post procedure arrangements – family, work.
- "Tracksuit" or similar clothes
- Suitability for Clexane – DVT prophylaxis.

Procedure Planning and Equipment

- 21g Needle (knee) – Syringe Shield
- Joint Access (Haemarthrosis – clotting factors)
- Steroid- Methylprednisolone (40mg) or Triamcinolone
- Marcaine (0.25%) or lignocaine (1 or 2%)
- Compression bandage
- Splint – Wheelchair - Crutches
- Follow-up (Phone Call and Clinical Review)
- Some patients will need aspiration and steroid injection 2-4 months post

Injection Protocol – Knee Y90

- Local Anaesthetic to skin 25g (orange needle)
- 21g puncture of supra-patellar bursa
- Non Luer Lock Syringes
- Aspirate joint to a 5-10 mls estimate residual volume – Always send Culture Sample
- Radioisotope in 1-2 mls – avoid skin spillage – back pressure control
- 40mg Depomedrone (or Triamcinolone)
- 3 mls 1% Local Anaesthetic
- Compression bandage

Non Luer Lock Syringe

Luer Lock

Non –Luer Lock


Einweg-Makrolonring, steril
Artikelnummer: 3191764
Abstandhalter zur Verringerung der Strahlen-
belastung durch betastrahlende Nuklide.
Verwendbar bis: 07/2009
CIS bio GmbH
Alt Moabit 91 d
10589 Berlin
cisbio

Joint Immobilization

- Donjoy Splint (or similar) – 15 degree flexion
- Koch Splint
- 48 hours immobilization
- Clexane 20mg s/c


KNEE

Volumes

- Modder Practice – 6,000 patients/year

  (Estimate 70,000 joints per year in Germany in 2008)

- Includes Inflammatory Osteoarthritis in large practices
  – indications change 70% osteoarthritis 30% RA
- 50% in knees
- Most European and USA large centers – 2 procedures/month

Radiation Protection – Beta Emitters

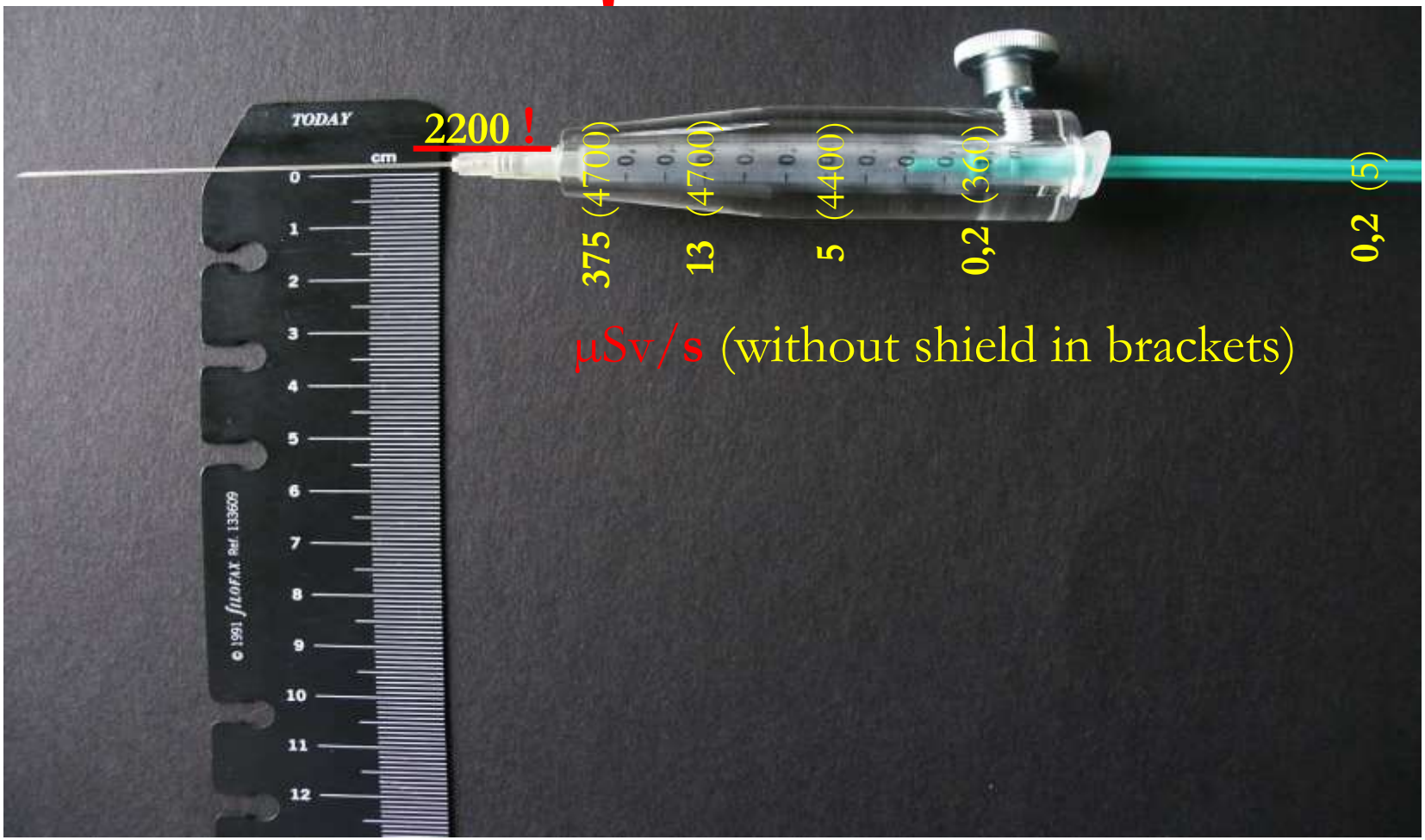
- Low Z shielding material such as Perspex
- Perspex/Lucite shield should be thicker than the maximum beta particle range
- Specialised syringe shields
- Make sure syringe shield can fit into Manollo ring
- Needle contact "constricted" slightly by Manollo shield
- ? Vinyl gloves
- B- finger dosimeter – inside left ring finger (right handed operator)

Radiation protection related features *)

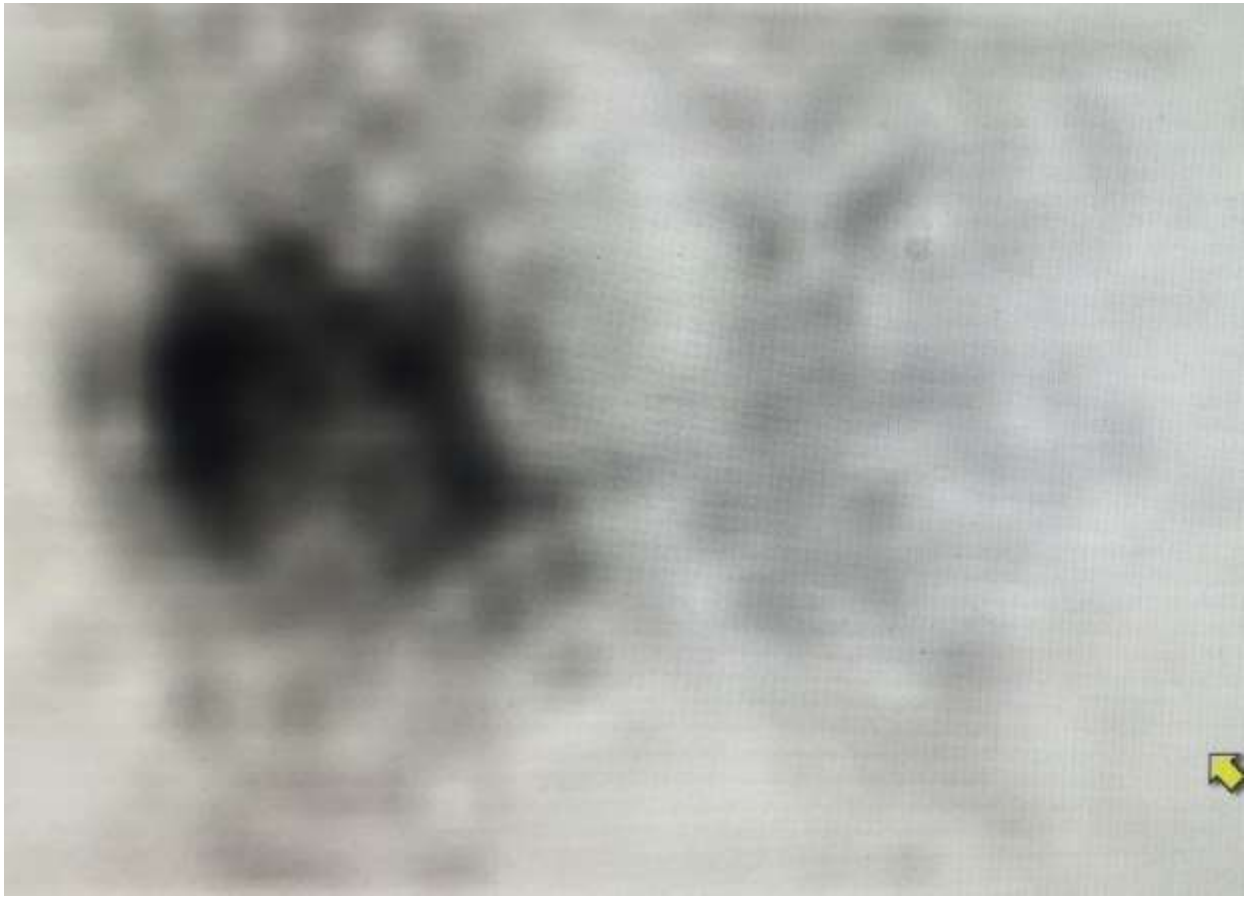
	Y-90	Tc-99m
Maximum / mean beta energy:	2.3 / 0.9 MeV	
Maximum / mean range in plastic:	9.2 / 4.0 mm	
Dose rate for 1 GBq:		
- in 30 cm distance from point source	120 mSv/h	0.3 mSv/h
- on 5 ml plastic syringe (surface)	**10 mSv/s !**	0.1 mSv/h
Dose rate for 1 MBq skin contamination:		
- 0.05 ml droplet with 1 MBq	**1350 mSv/h**	8.8 mSv/h

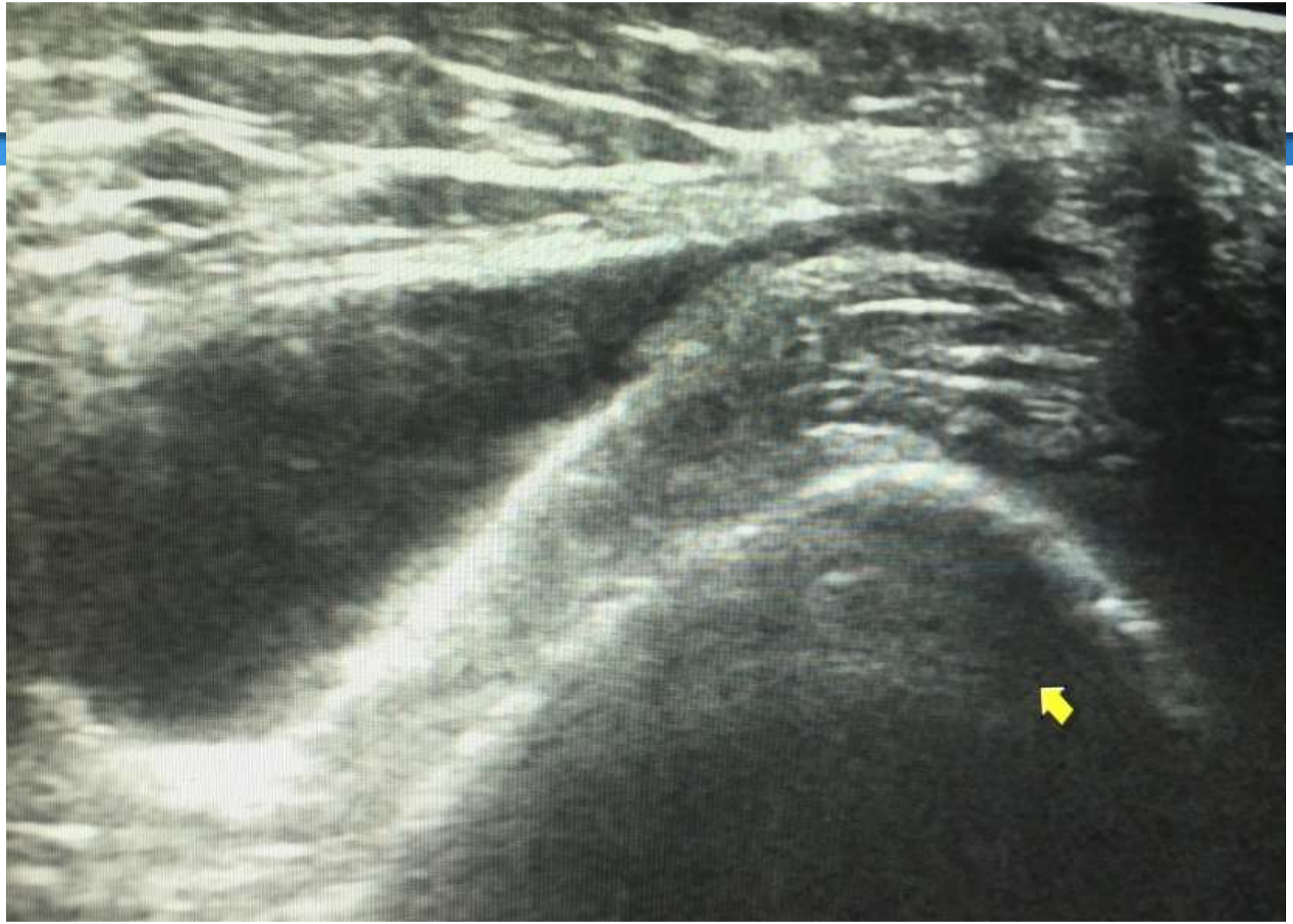
*) Delacroix D., Guerre J. P., Leblanc P., Hickman C. Radionuclide and Radiation Protection Data Handbook 2002. Rad. Prot. Dosim. 98, Nr. 1, (2002).

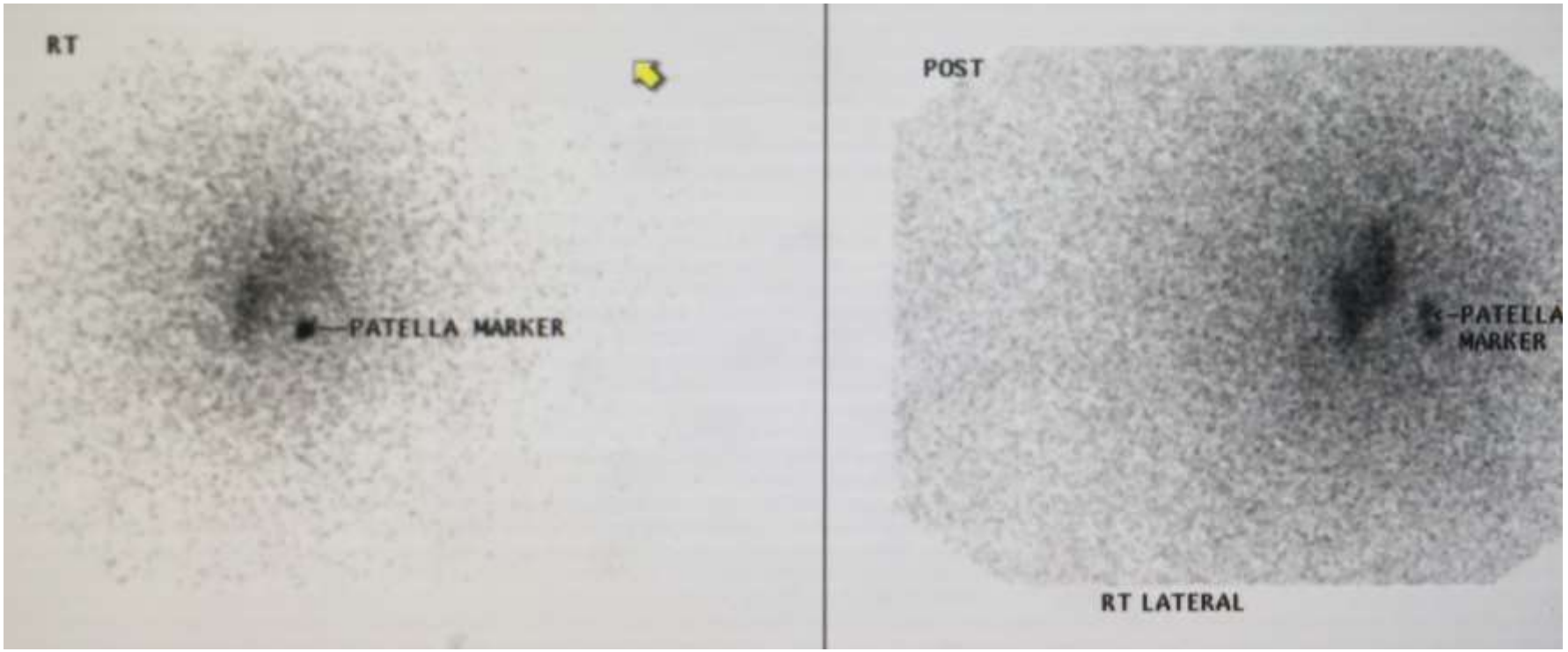
Dose rates
(for185 MBq Y-90)

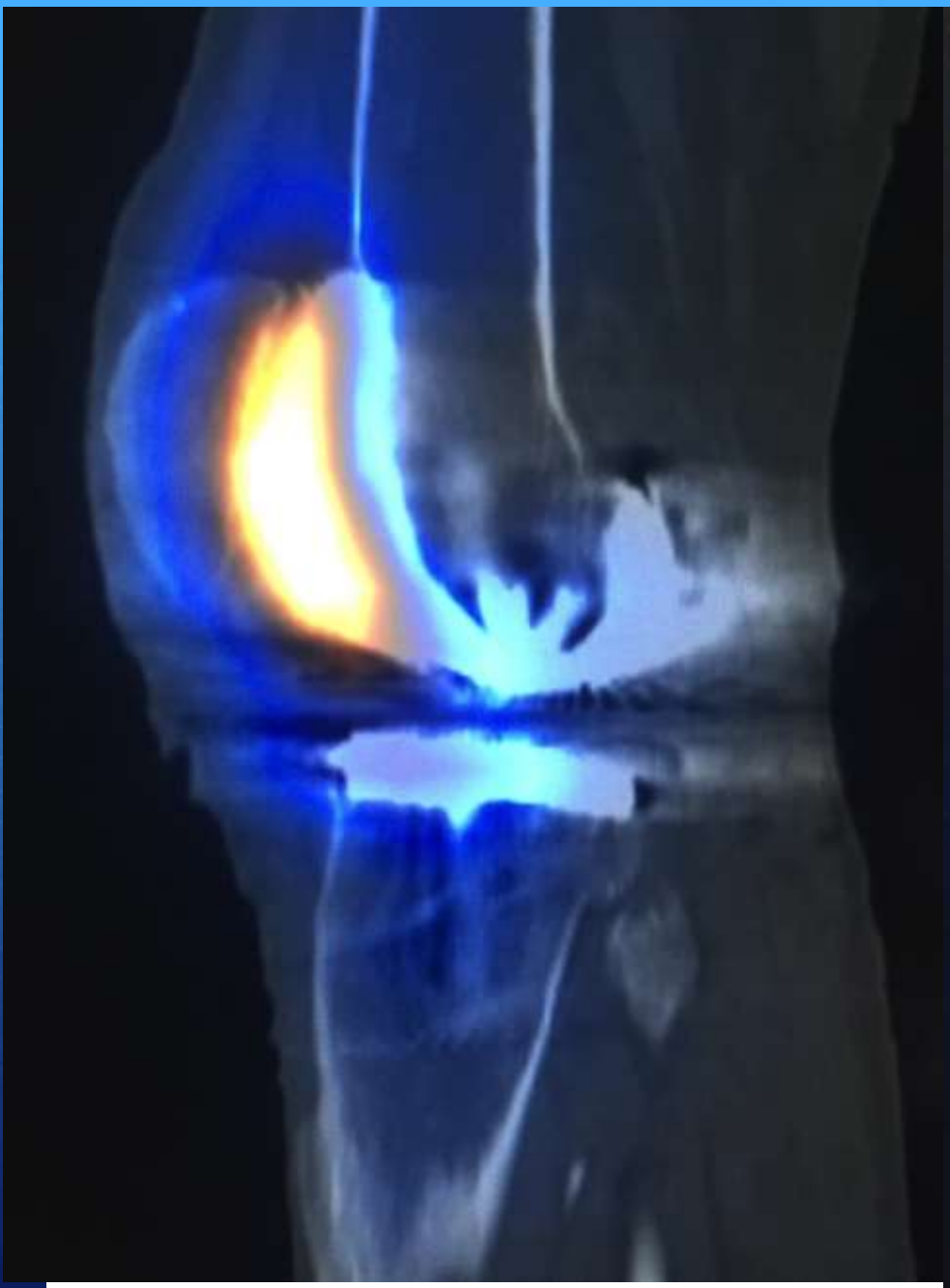


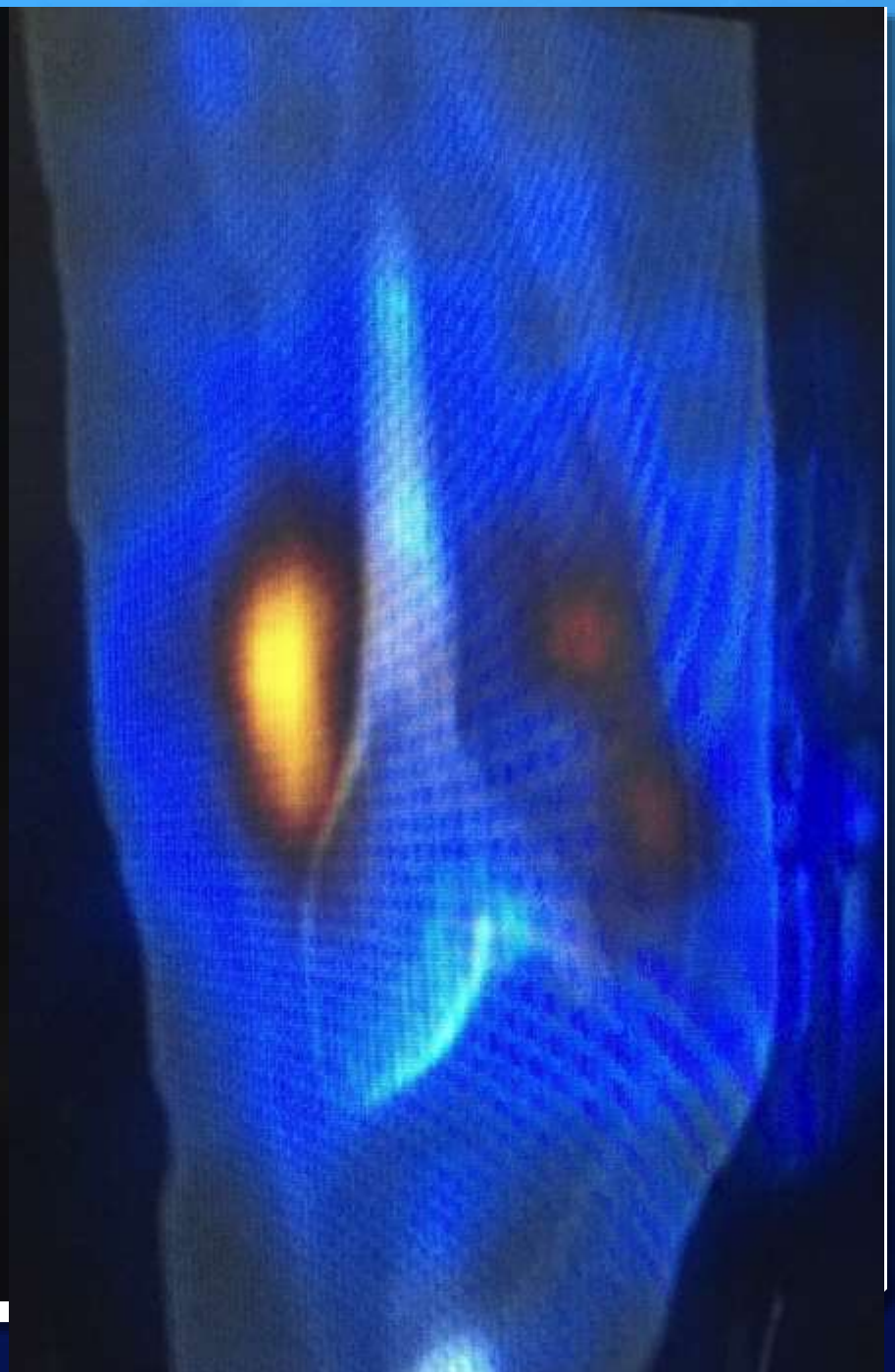
Bone Scan assessment – patient selection

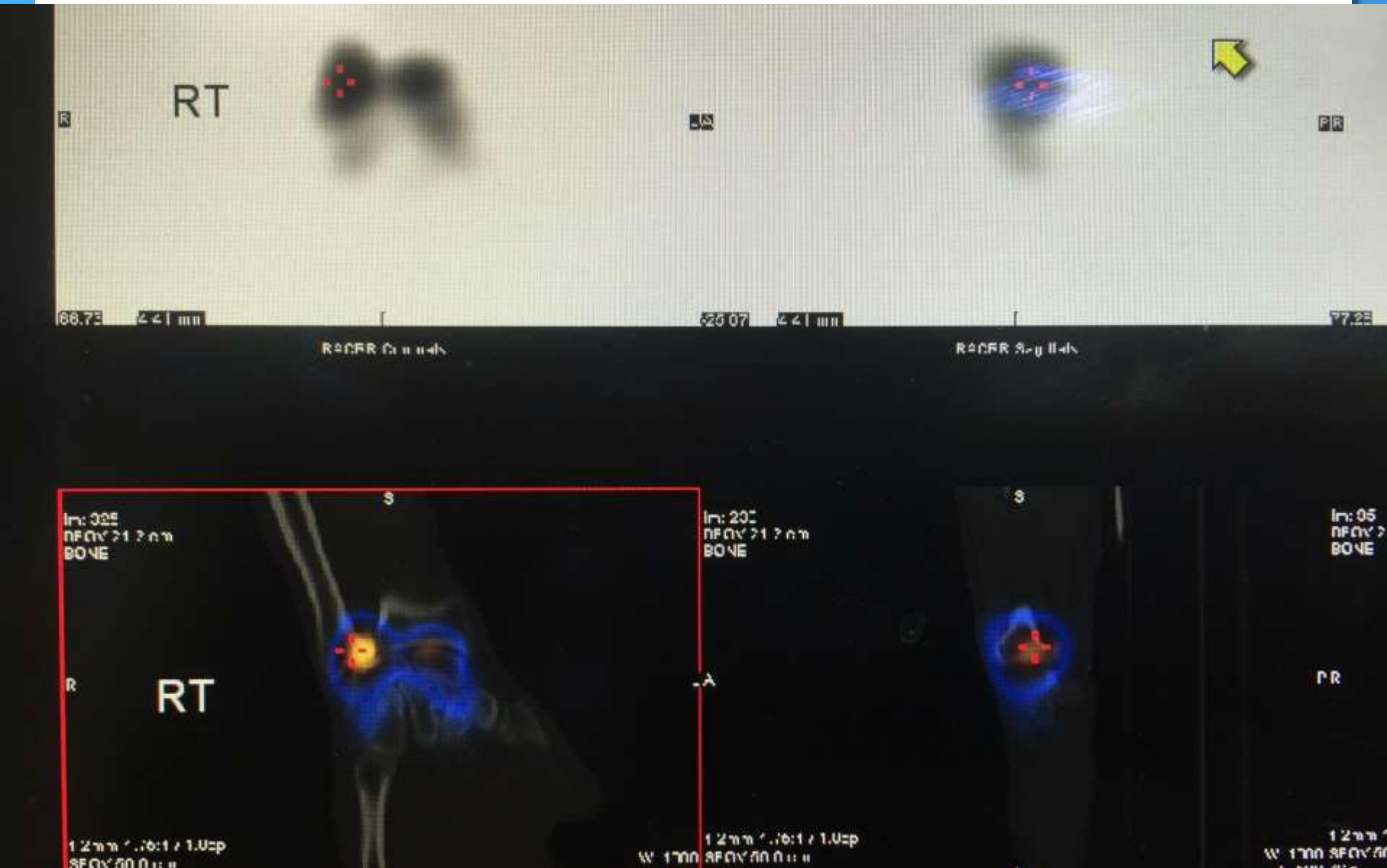





RT
PATELLA MARKER
POST
PATELLA MARKER
RT LATERAL






RT
RT
BONE

Contrast in Radiosynovectomy

- In vitro, large volumes of contrast can cause Radionuclides to dissociate from colloids
- Use smallest volume of intra articular contrast to confirm intra-articular position

  (Schmomacker et al 2005)

- Not needed in the knee

Follow-up and Joint Aspiration Post Radiosynovectomy (knee)

Call patient 4 days post injection?

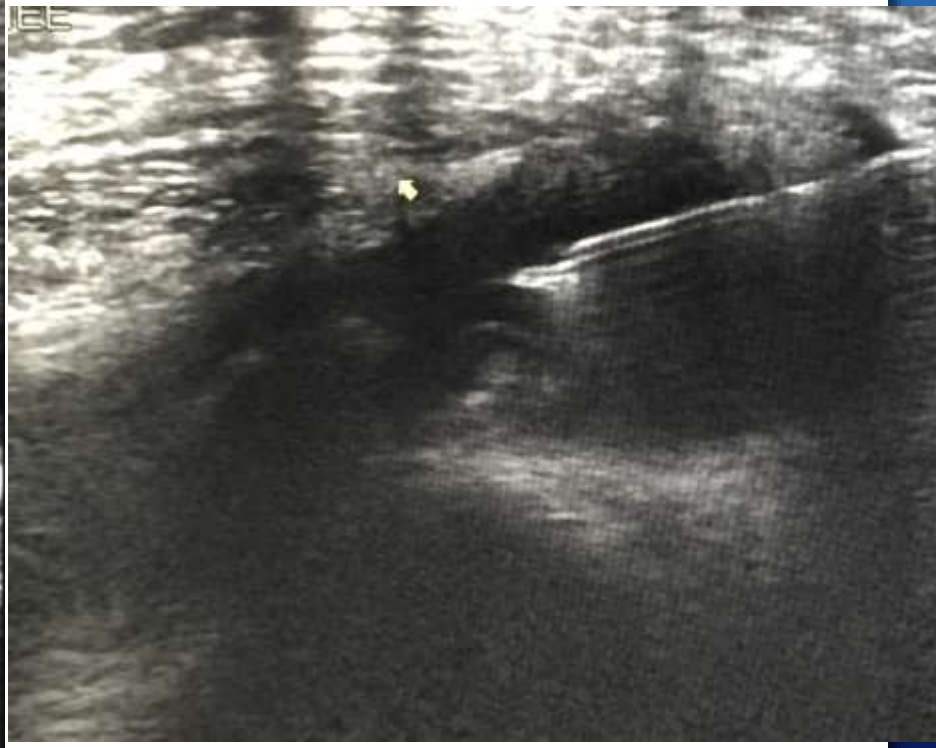
Avoid aspiration at less than 1 month post injection where possible

Often Significant clinical benefit from aspiration and steroid – 3-4 months after procedure ideal – more gel like

Contra-indications

- Pregnancy/Breast Feeding
- Local Skin Infection
- Rupture of Baker's Cyst or high tension Bakers cyst with valve mechanism
- Extensive Joint instability with bone destruction
- RSO under 20 years of age – Risk/Benefit e.g. 15 year old knee PVNS

Baker's Cyst (25%) – should drain if a valve mechanism



Our experience – 2 institutions

- 24 patients in 10 years
- 27 treatments
- 6 treatments not of the knee – 3 elbow, 3 wrists
- Knee average dose 185 MBq Y90
- 148 MBq in knee prosthesis
- Age 32 to 74

Indications in our practice

- PVNS (n=5)
- Psoriatic arthritis (n=3)
- Symptomatic Knee prosthesis (n=3)
- Non specific Monoarthritis (n=5)
- Seronegative arthritis (n=5)
- Rheumatod Arthritis (n=3)

Costs

- E.g. Cost: 226 MBq Y90 is

  226 Euros plus VAT and delivery

- Staffing :

  Radiologist or Nuclear Medicine Physician

  Senior Medical Physicist (s)

  Radiographer

- Steroids, Splint, Post procedure SPECT/CT

Results

Results (Our experience) – 27 treatments

- 2 proven infections – elbow- Rhenium, Knee Y90 with prosthesis
- 1 infection not proven at culture at 2/12, but infection 8 months post procedure – classic Staph Epidermidis
- 11 patients experienced significant response in 13 procedures
- 4 no improvement
- No follow-up data on 9 patients and 10 procedures
- We don't know our response rate!

Efficacy in the literature

- 60-80% of patients benefit
- Response at 1-3 months, unlikely in first 2/52
- Temporary increased synovitis
- Efficacy may be a reduction in other medications
- Efficacy – how to measure – scintigraphy may be an accurate reproducible method

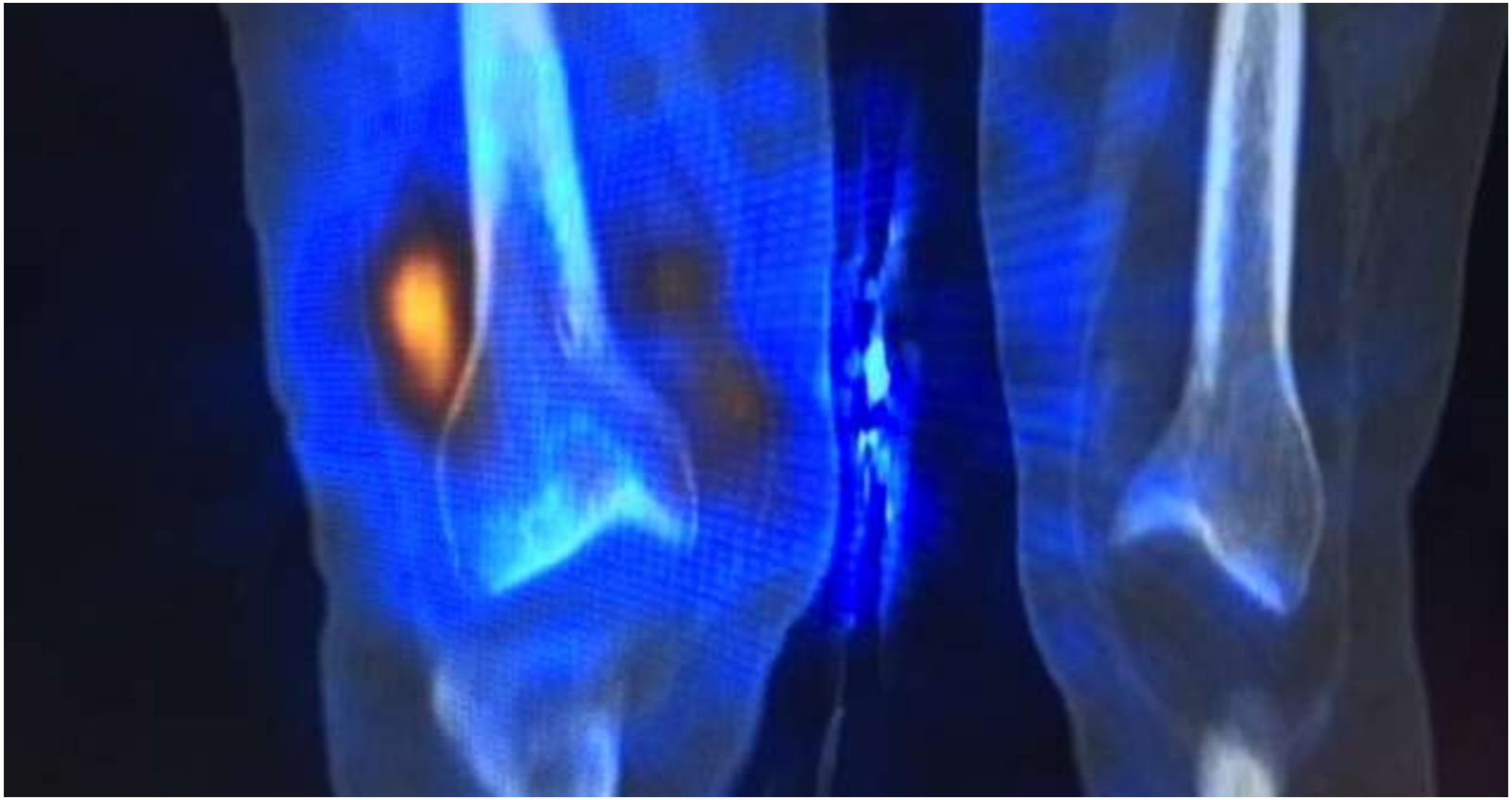
Response Rate

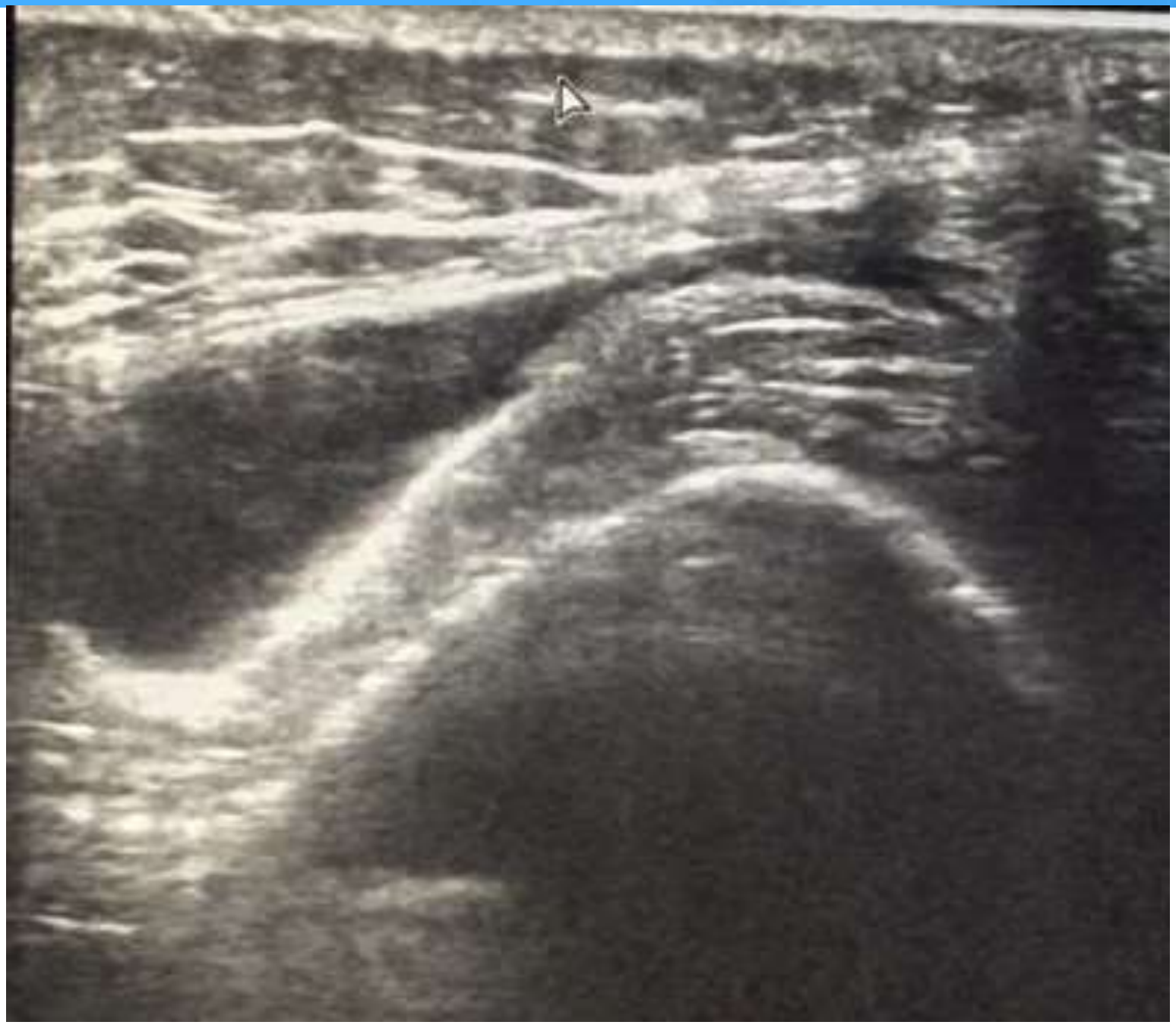
- More effective in RA than OA
- RA: Steinbrocker Stage I and II respond better than stages III and IV
- 40% response rate in severe OA (Kroger et al 1999)
- 2190 patients over 28 years, overall response rate 72.5% (Kresnik et al 2002)

Patient Comments from our practice

- "Improved but still have joint swelling"
- "Great, much better"
- "Not as painful, don't need as much anti-inflammatories"
- "No effect"
- "Initial response, now just as bad"
- Five patients requested another joint to be treated (n=3 knees), Same joint (n=1) or Same joint, but was declined (n=1) due to previous external beam irradiation

Case 1: Non specific Arthritis





Case 2 PVNS pre Debulking

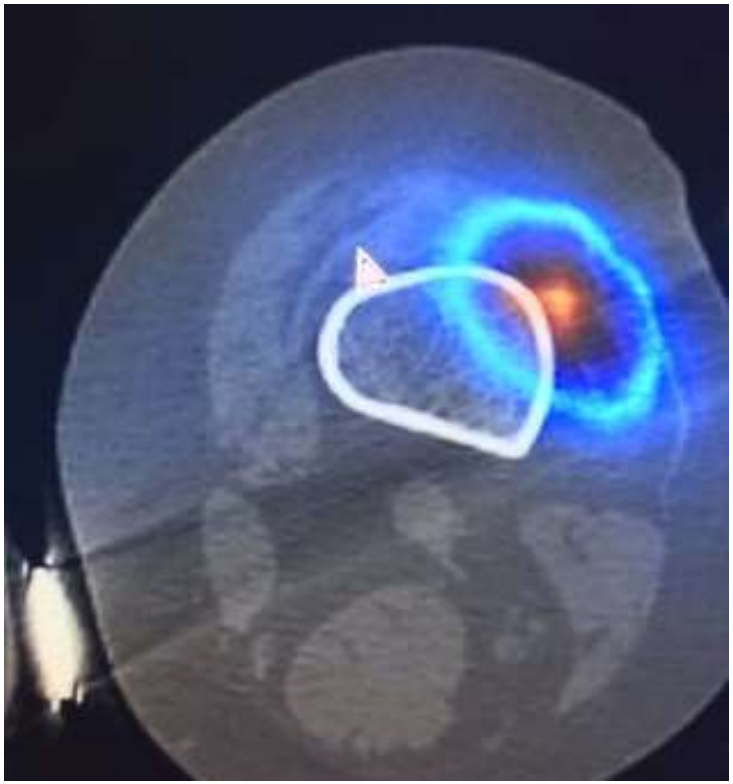
PVNS

- Pigmented Villonodular synovitis
- Characteristic MRI appearance – destructive arthritis with slowly progressive benign proliferation of synovium
- Very rare – 2/million
- Arthroscopic de-bulking but with relapse rate, 8-46%
- External beam Radiation?

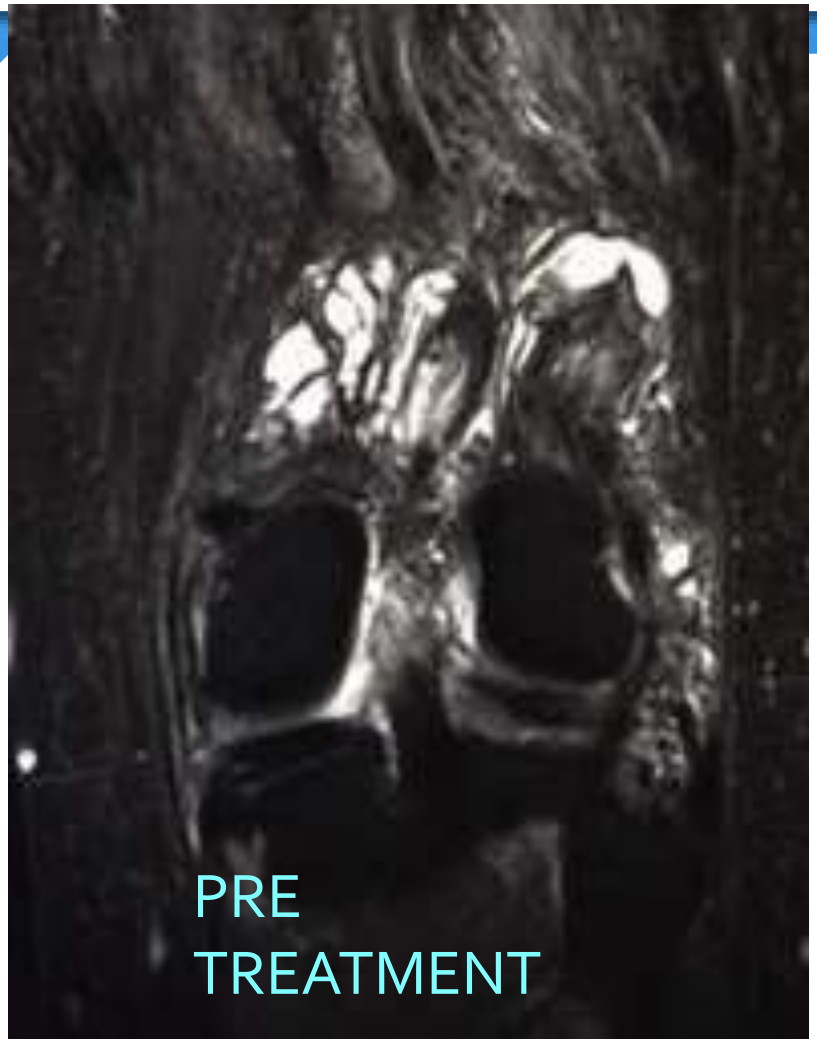
PVNS - Radiosynovectomy

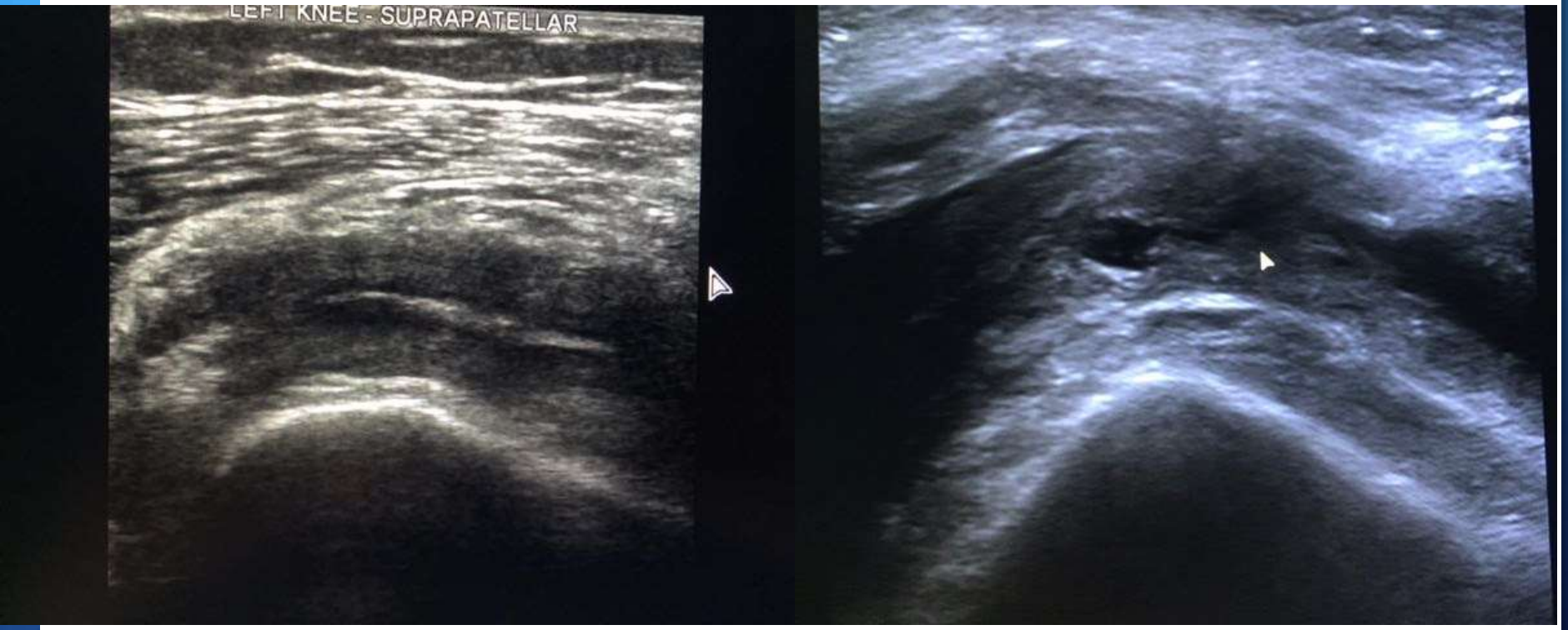
- 6 weeks post arthroscopic synovectomy
- Blind spots
- External beam radiation may make total treatment dose calculation difficult


LEFT KNEE



Posterior Joint Space




LEFT KNEE - SUPRAPATELLAR

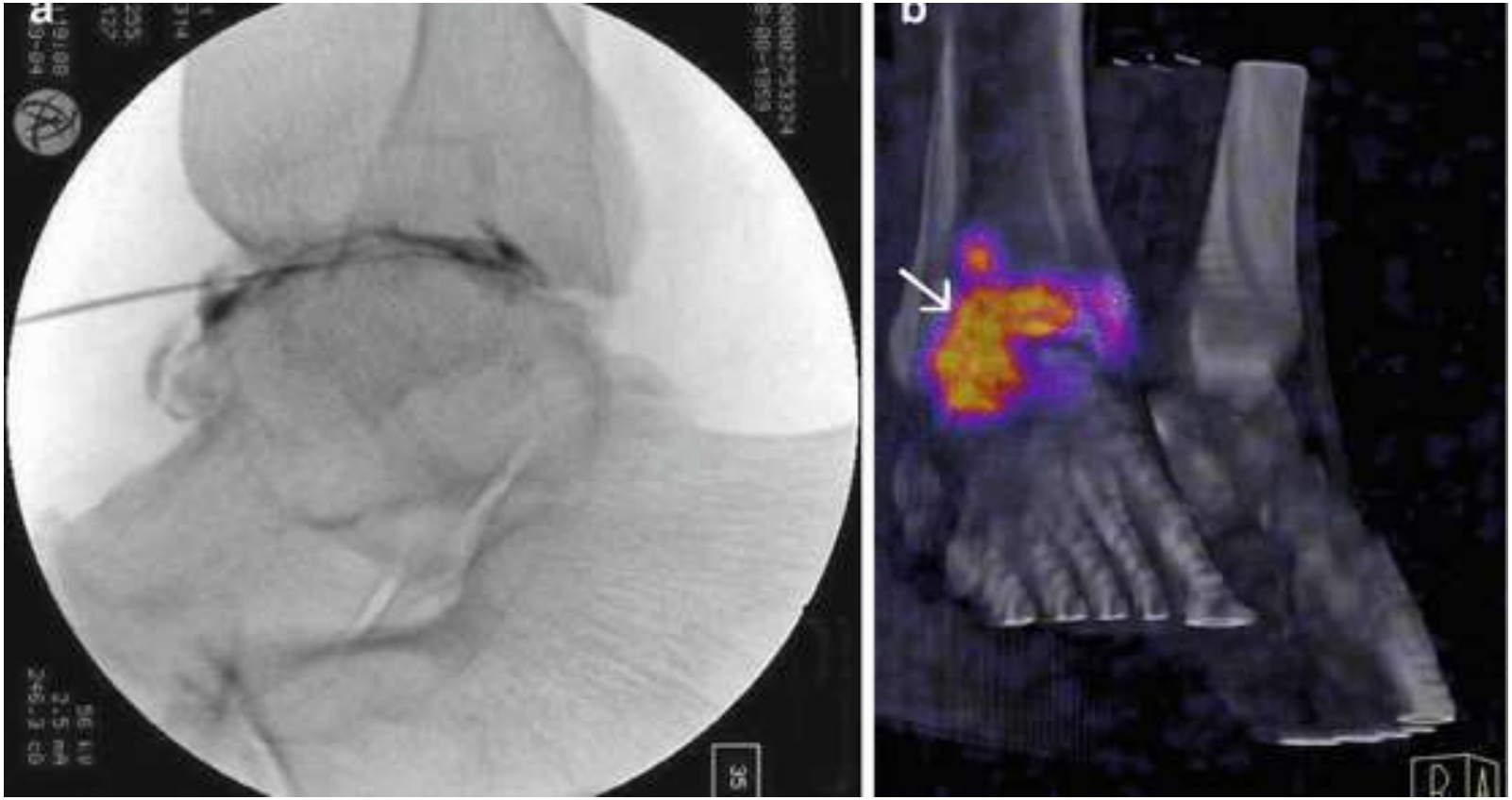
Haemophilia

Prevent long term arthritis by managing acute haemorrhages aggressively

Recurrent bleeding with chronic synovitis does not respond to clotting factor replacement

Surgical synovectomy option obviously challenging – extensive clotting factor replacement, limited range of motion, prolonged hospitalization

Haemophilia Radiosynovectomy - Rhenium



Prosthesis Synovectomy

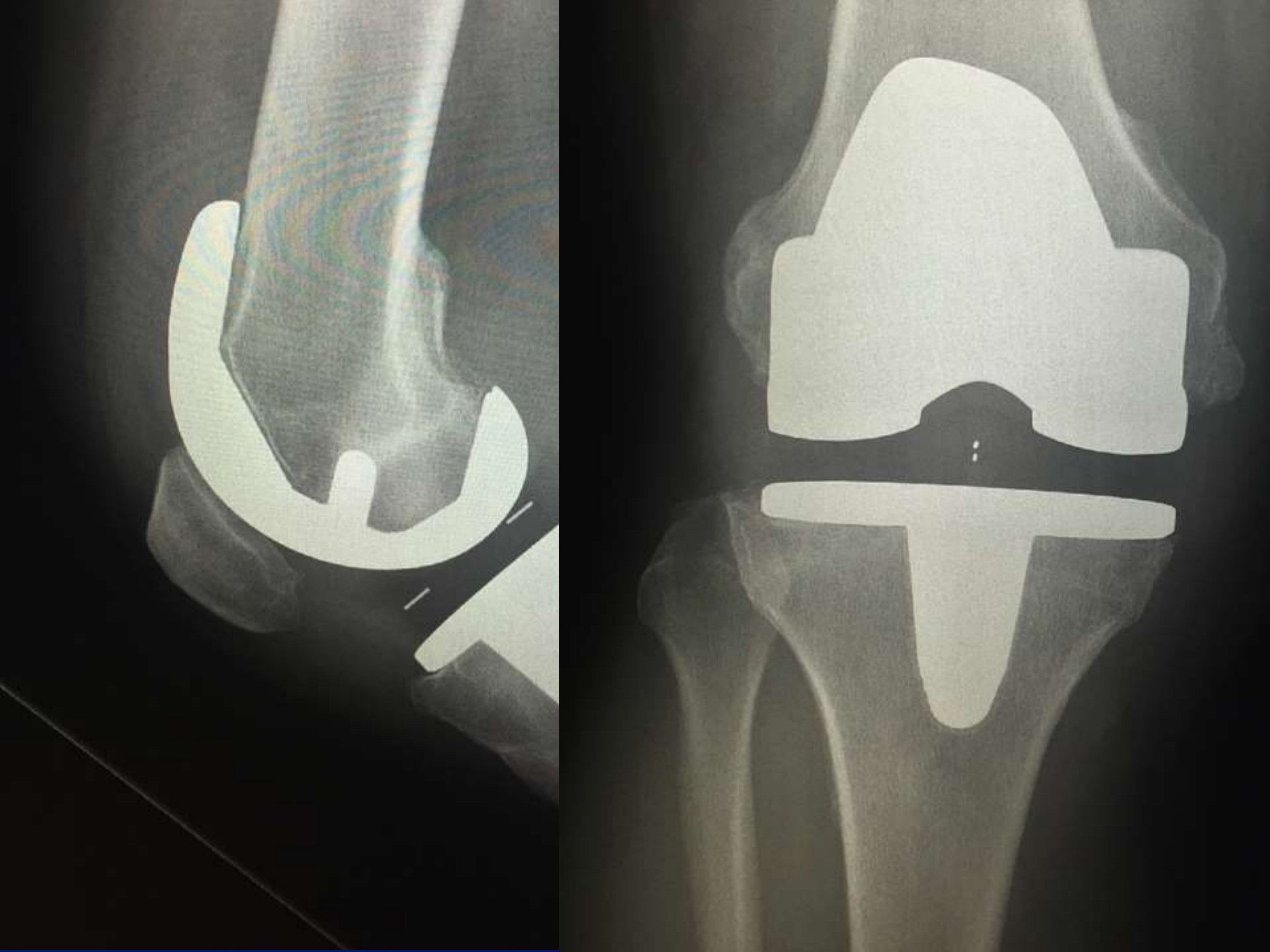
- Lower dose used- 3mCi

(Modder treats twice – now using higher doses 5mCi first, 6mCi second at 3/12)

- Our experience is with knee prosthesis
- No significant response (n=3 knees) - ? Dose selection
- Role in particle disease
- "flush" a bloody effusion until clear
- Modder: "Treat with care" – very good results

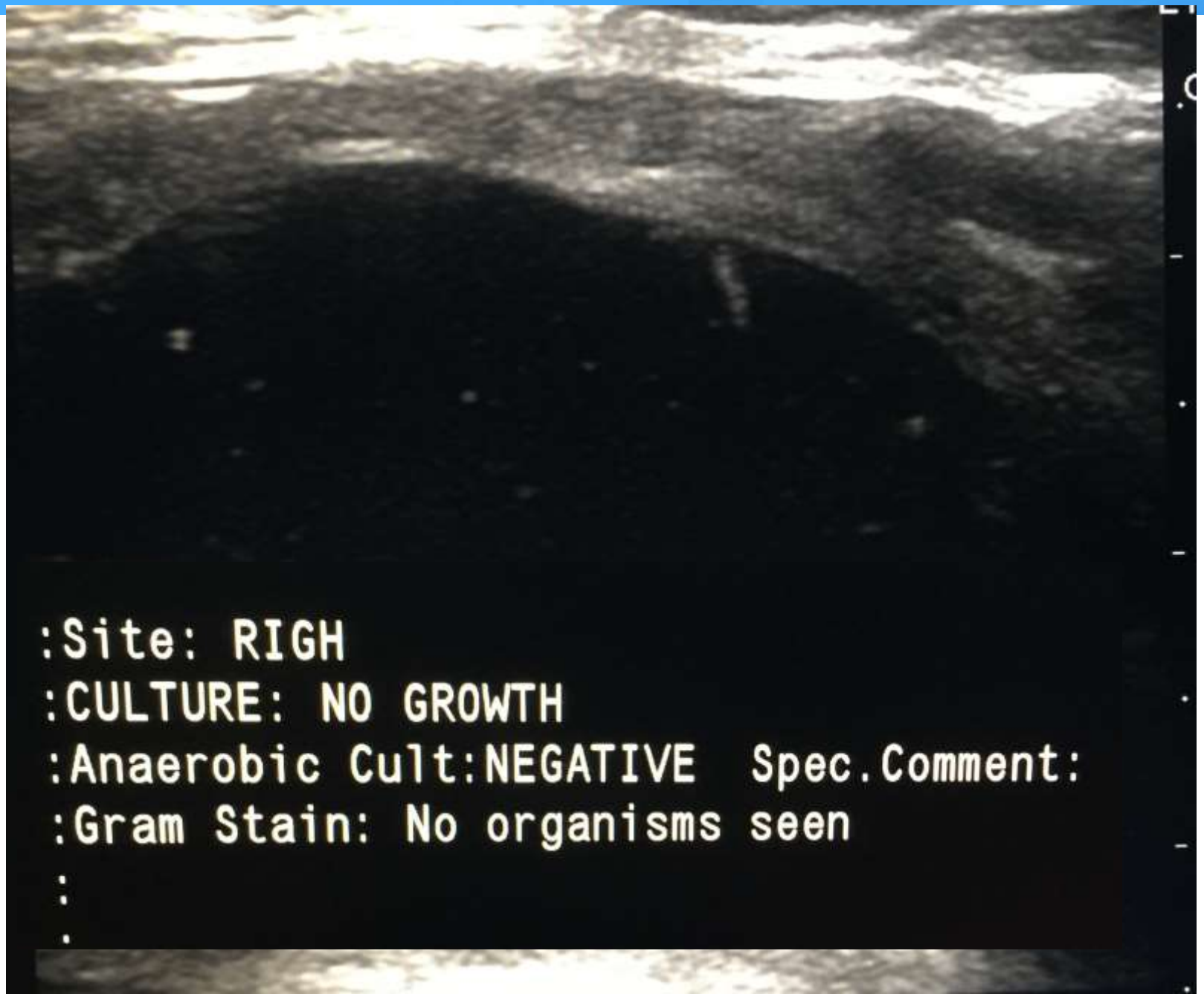
Complications:

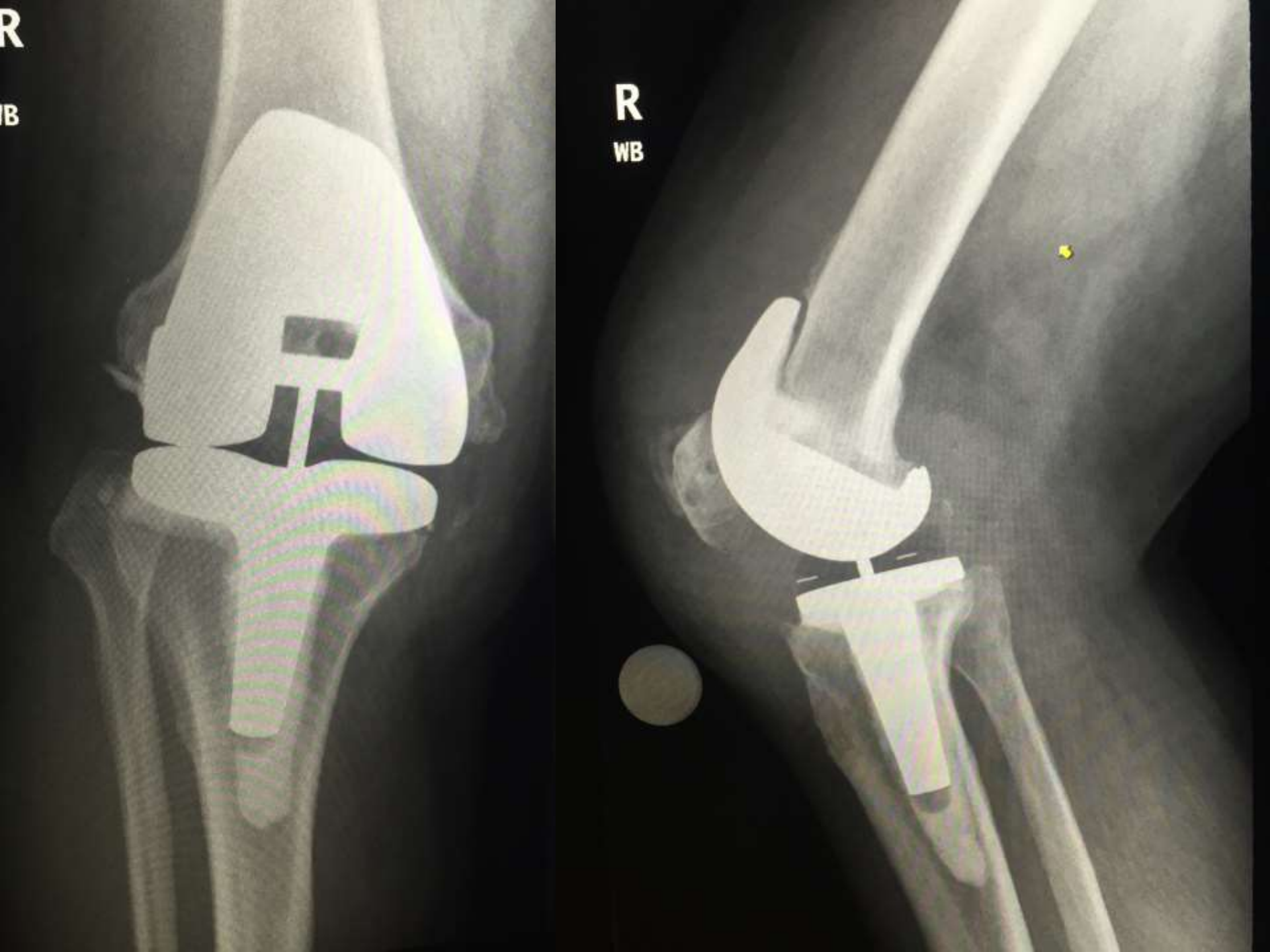
- Infection
- Extravasation




01-Jul-1952 64


501
01-Jul-1952 64


:Site: RIGH
:CULTURE: NO GROWTH
:Anaerobic Cult:NEGATIVE Spec.Comment:
:Gram Stain: No organisms seen


R
WB


R
W/B

Factors that might make infection more or likely

- Transport and multi focal handling of isotope increases possibility of contamination.
- Activity measured in sterile vial, but must be accessed in fume cupboard x 2 – at initial source and in treatment hospital to administer target dose – not GMP?
- Immobilization of joint?
- Ultrasound room administration – non sterile
- Extra substance compared to conventional arthrogram proecdures
- Radioactivity should reduce bacterial count?
- Modder et al: 1 infection in 4000 knee injections – B irradiation destroys bacteria
- **Our experience is that Y90 does not destroy bacteria**

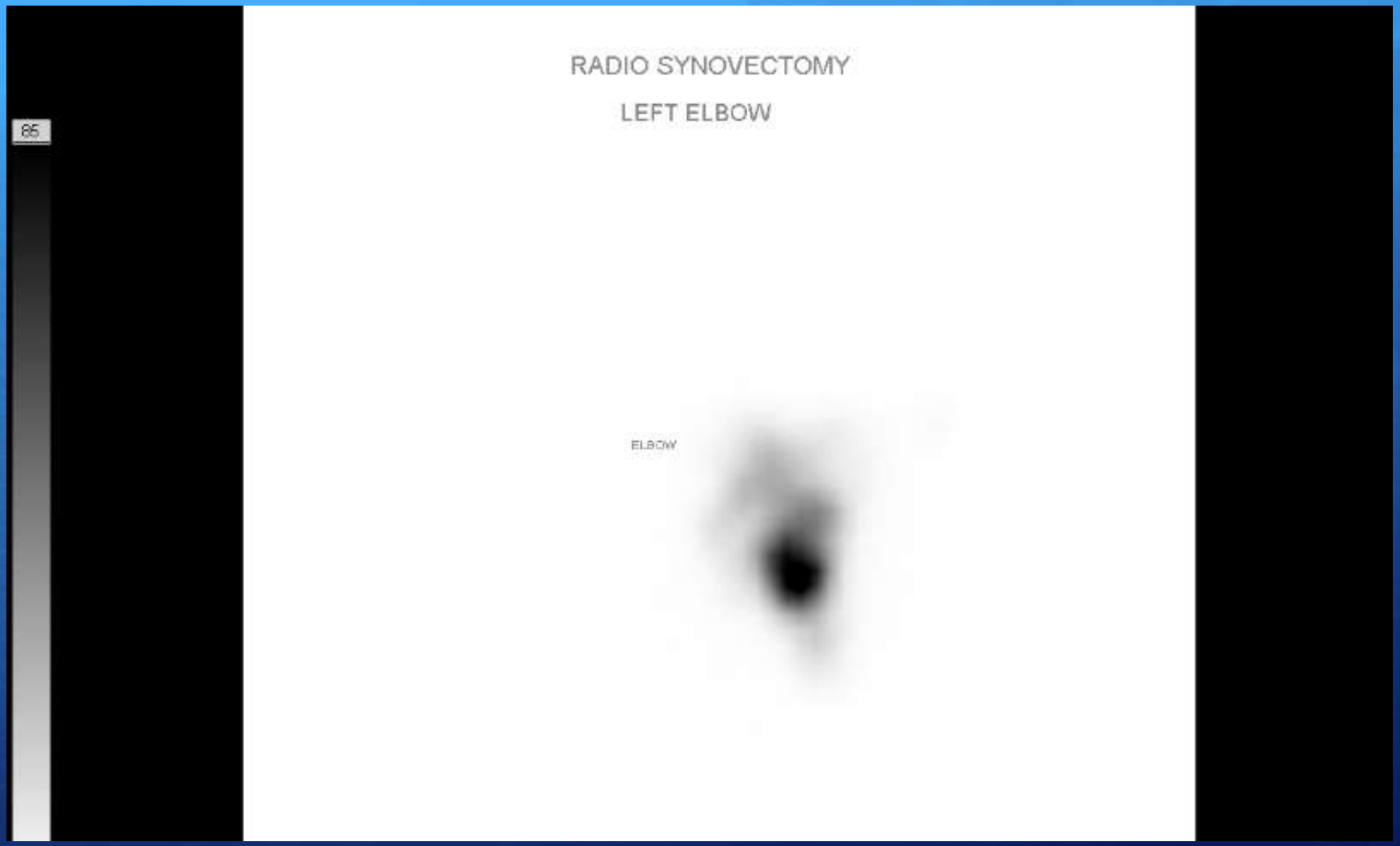
Knee prosthesis failure in Orthopedics

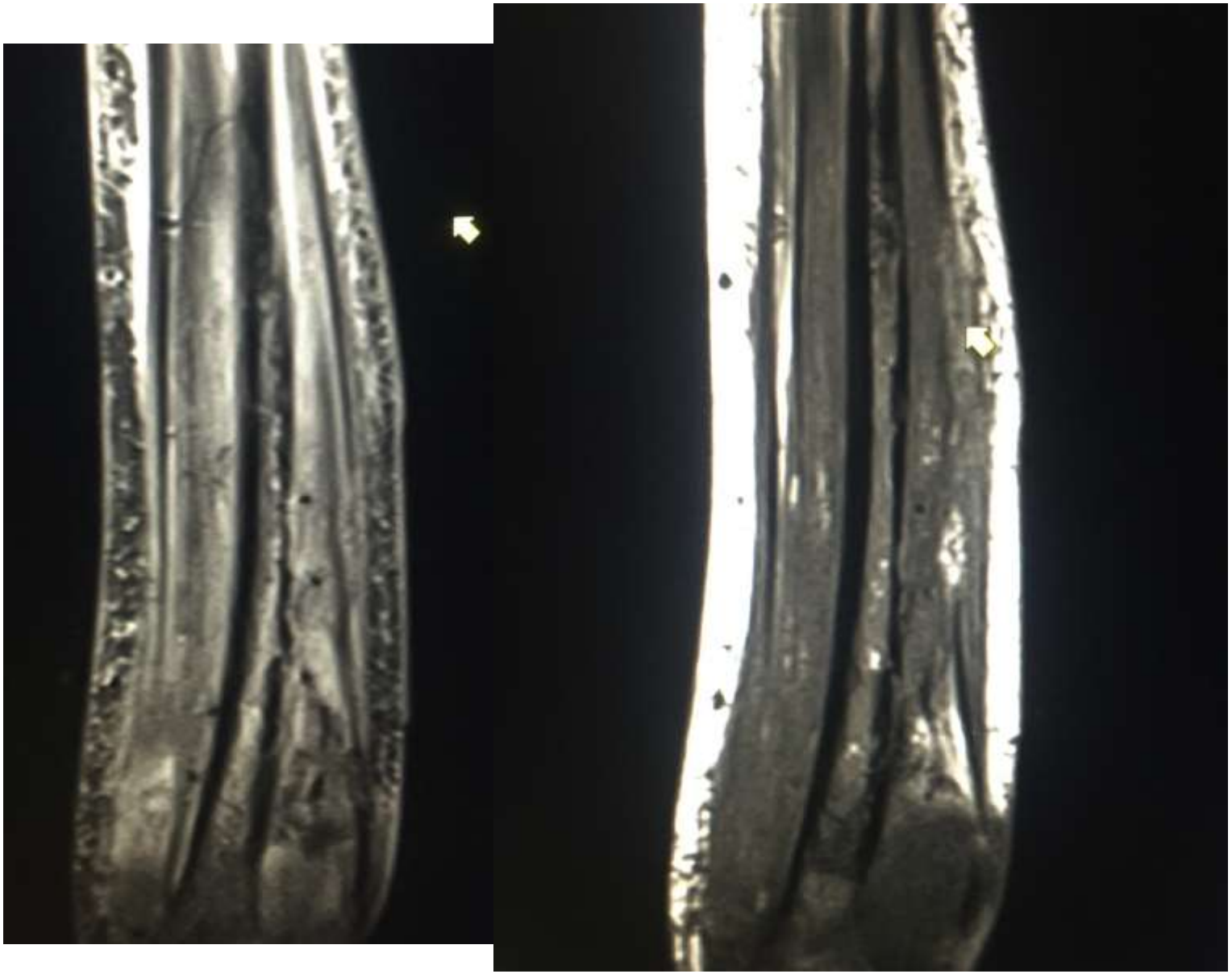
- High rate of Staph Epidermidis colonization of polymer surfaces – "Gel like" coating of surface of implant
- Polyethylene wear leading to aggressive granulomatosis
- In an unexplained prosthesis failure many orthopaedic surgeons will now assume infection and will treat with PICC + antibiotics for 6 weeks, pre prosthetic replacement, with/without antibiotic spacer


UP

RADIO SYNOVECTOMY

LEFT ELBOW





Extravasation of Radioisotope (General Radioisotope Advice)

- "You don't" (Big John) – Prevention
- Site important
- Most experienced operator

General Advice for Therapeutic Isotope Extravasation:

Aspirate first

Then flush with sterile saline – increases absorption

Elevate and apply heat

Unacceptable Complications Following Intra-Articular Injection of Yttrium 90 in the Ankle Joint for Diffuse Pigmented Villonodular Synovitis

Jacob Bickels, MD[1], Josephine Isaakov, MD[1], Yehuda Kollender, MD[1] and Isaac Meller, MD[1].

Background: Simple resection of diffuse pigmented villonodular synovitis of the ankle joint is associated with local recurrence rates as high as 50%. Thus, adjuvant treatment modalities, such as radiation or intra-articular isotope injection, are sometimes used after tumor resection. Our initial and highly satisfactory experience with the injection of radioactive yttrium 90 to treat pigmented villonodular synovitis of the ankle joint eroded with time so much so that we discontinued its use in the ankle and believe that it is important to alert our colleagues to the complications that we observed. Methods: Between 1989 and 2006, we treated seven patients who had diffuse pigmented villonodular synovitis of the ankle joint with subtotal synovectomy followed by intra-articular injection of 15 mCi of yttrium 90.

Results: Two of the study patients had full-thickness skin necrosis develop around the injection site, necessitating free muscle flap transfer within three months of treatment, and a third patient had development of a draining sinus that was associated with chronic severe pain. The other four patients reported pain after the injection that was reasonably controlled by the use of nonsteroidal anti-inflammatory drugs. At the most recent follow-up evaluation, no study patient had recurrent disease.

Radiation Necrosis Ulcer

Insurance coverage (private sector) and procedure practicalities

- Not covered by VHI (largest insurer in Ireland)
- Rheumatologist/Orthopaedic referral only
- Pre procedure imaging – eg. Knee ultrasound
- Ultrasound or fluoroscopic guidance
- Post procedure planar or SPECT/CT biodistribution
  - Tc99m window Brehmsstrahlung imaging
- Splint and crutches – wheelchair to door
- Time off work for immobilization

Under 20 years of age Radiosynovectomy?

- If benefit likely to out way potential hazards?
- Ozulker et al: 11 pts mean age 11.7 years for Haemophilic Arthropathy.

  Doses 4-5mCi Y90.

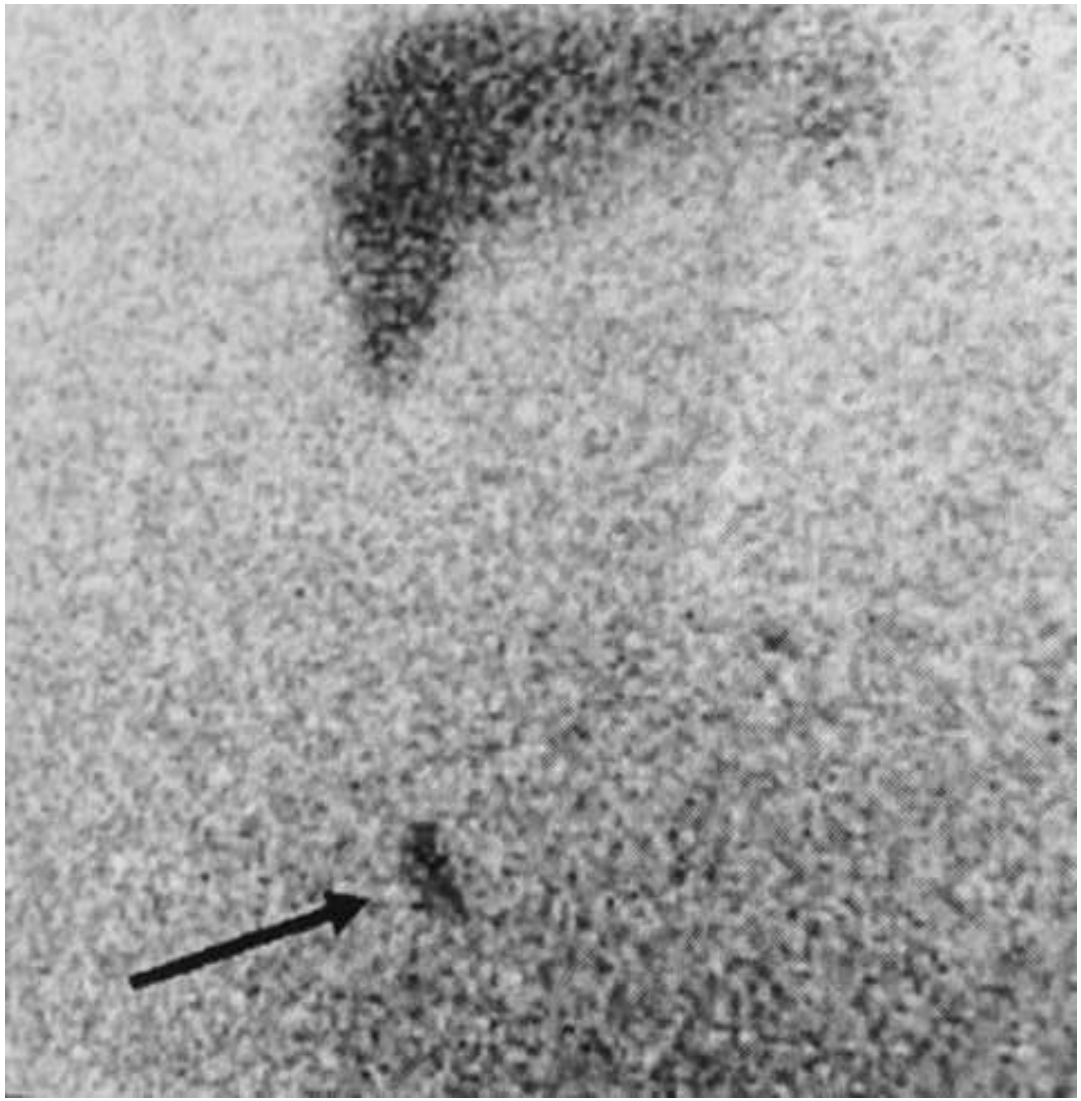
  54% improved frequency of Haemarthrosis

Modder says: 3mCi of Rhenium-186

Questions

- What is risk of infection?
- How effective is the technique? Don't have enough of our own data.
- Literature suggests it out performs steroids and for a longer period
- Is some benefit due to joint immobilization?
- Would we do more procedures if we had more time?

  Yes – but not with a prosthesis present



Malignancy Risk

Voth et al 2006

- Dicentric chromosomes in peripheral lymphocytes
- Pre RSO with Y90 – 0.25%
- Post RSO – 0.41%

Kos-Golja et al 1997

- Meta analysis 180 studies 9,300 patients with Y90
- 2 malignancies, CML at 4 years and CLL at 6 months (likely unrelated)
- One study detectable activity on whole body imaging in 15 of 35 patients – Klett et al 1999

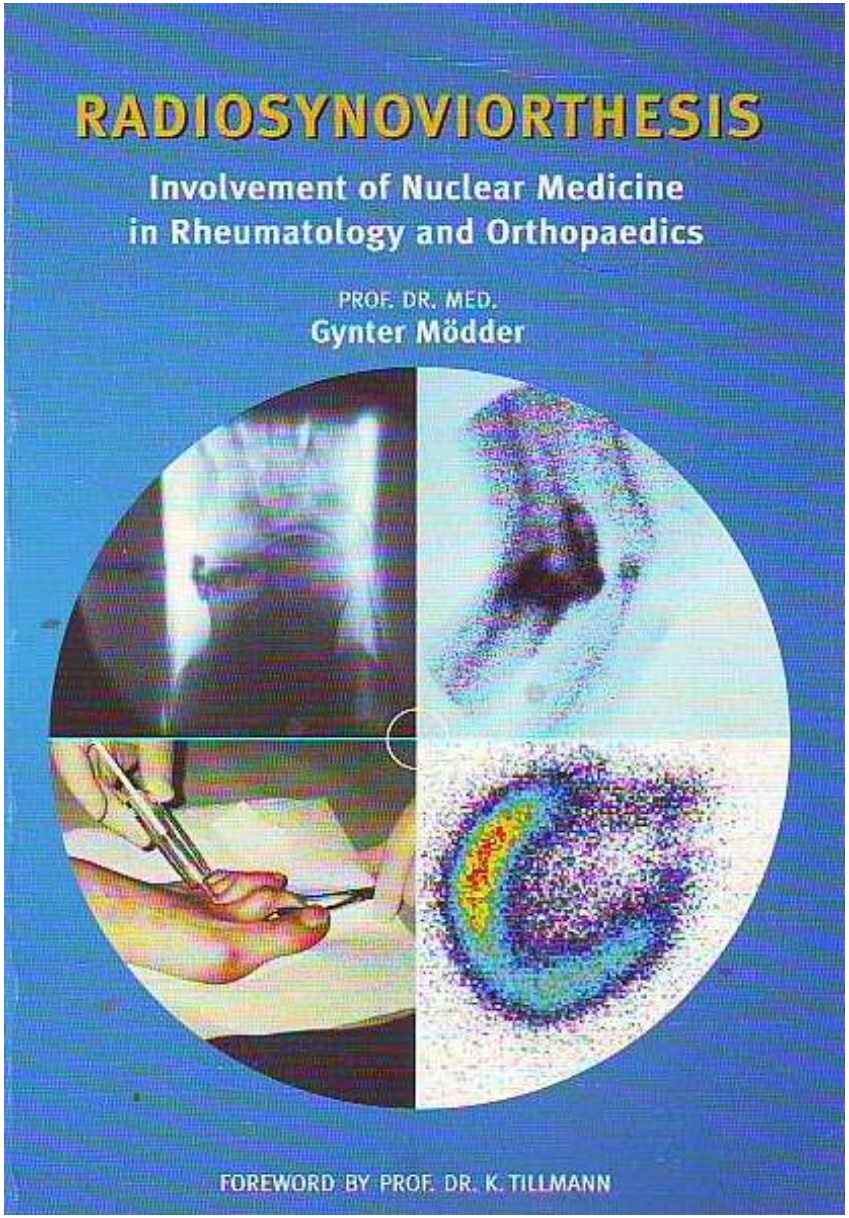
Radiation

- What we worry about is Radiation induced necrosis – only an issue with high doses of wrong isotope in wrong location
- What I previously worried about was "free" metal isotope ending up in the bone marrow
- No unequivocal reported cancer induction
- What I now worry about is infection?

? Stop worrying!

Conclusions:

- RSO widespread technique with potential to treat chronic disease safely with moderate efficacy
- Needs careful consideration for patient and staff safety, due to multiple hazard nature
- Dose limits to operator easily exceeded if proper precautions not followed
- Safe procedure with good protection practice
- Second aspiration and injection 2-4 months post knee procedure seems to benefit sigificantly, without radiation risk


RADIOSYNOVIORTHESIS
Involvement of Nuclear Medicine
in Rheumatology and Orthopaedics
PROF. DR. MED.
Gynter Mödder
FOREWORD BY PROF. DR. K. TILLMANN

INMA

Thank You

oconnellm@mater.ie