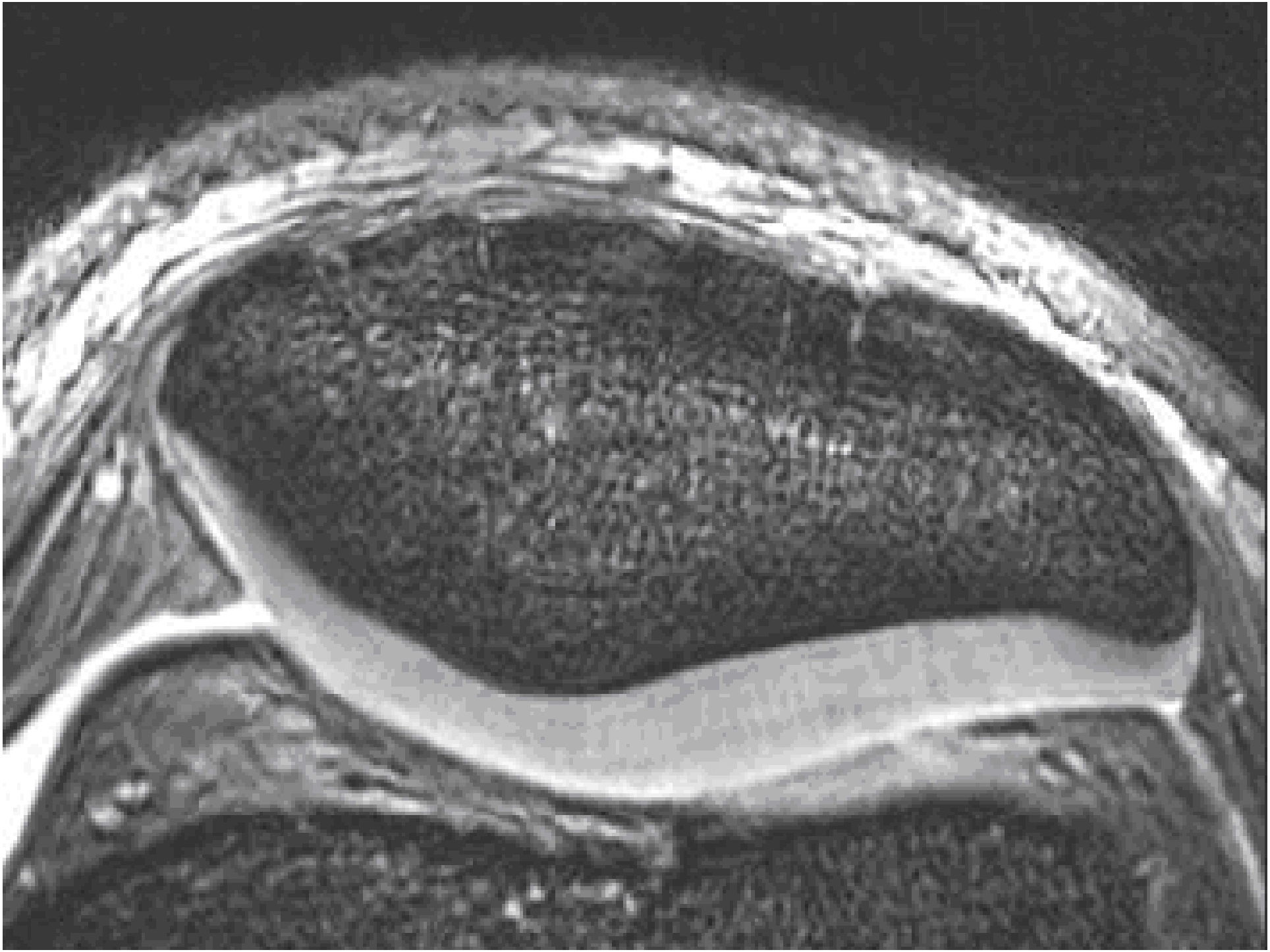
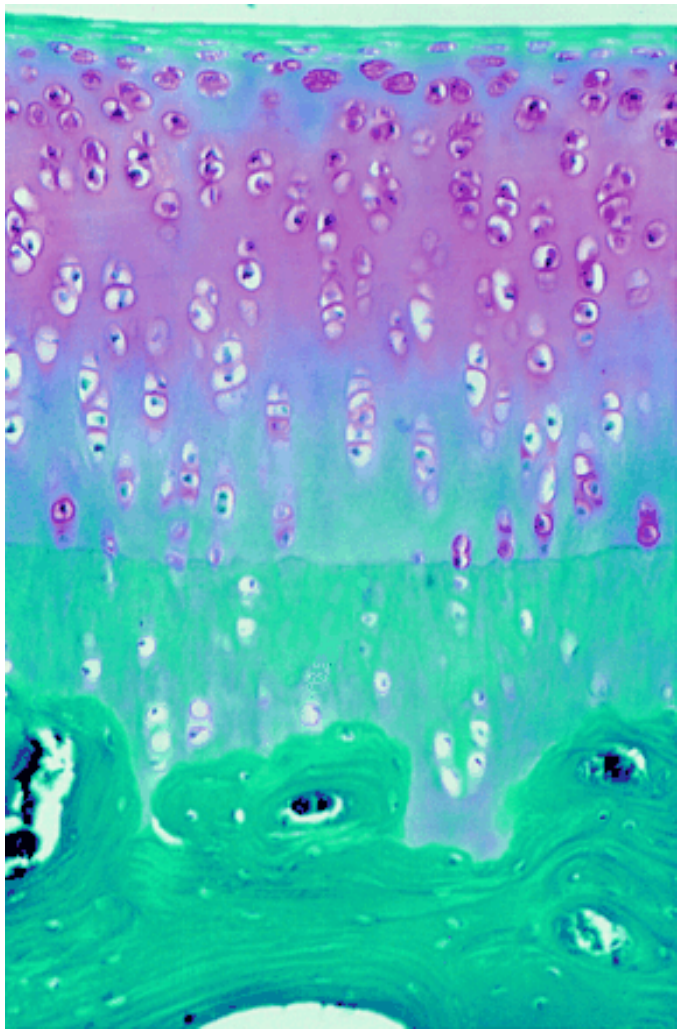
Autologous Chondrocyte Implantation

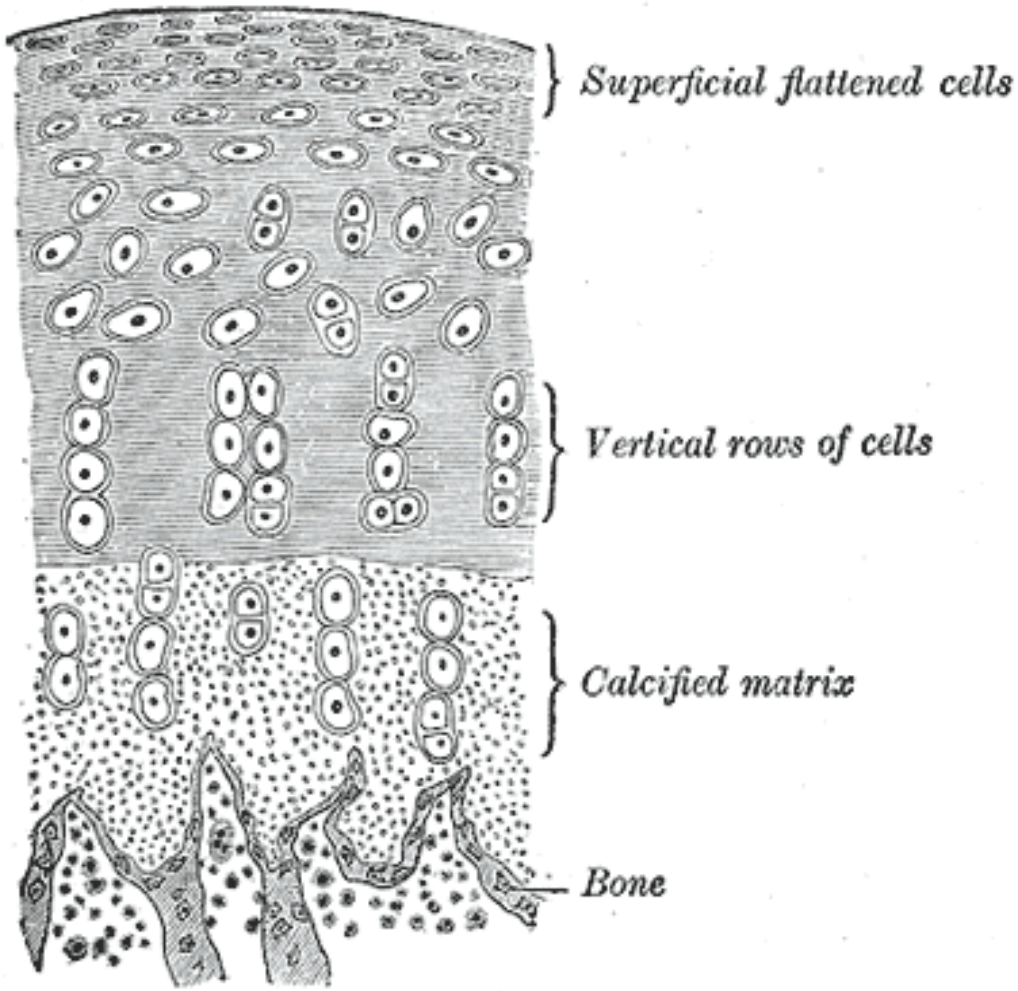
William Jackson

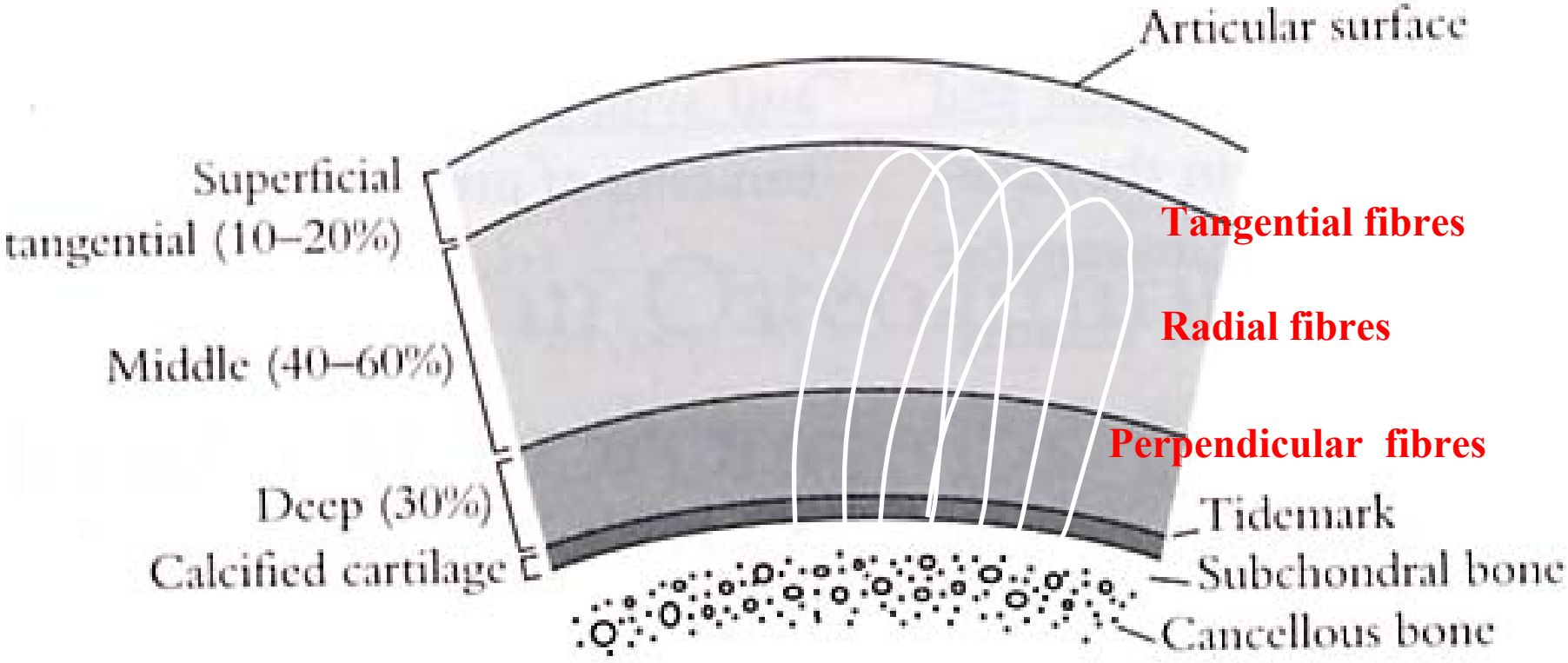
Consultant Orthopaedic Surgeon

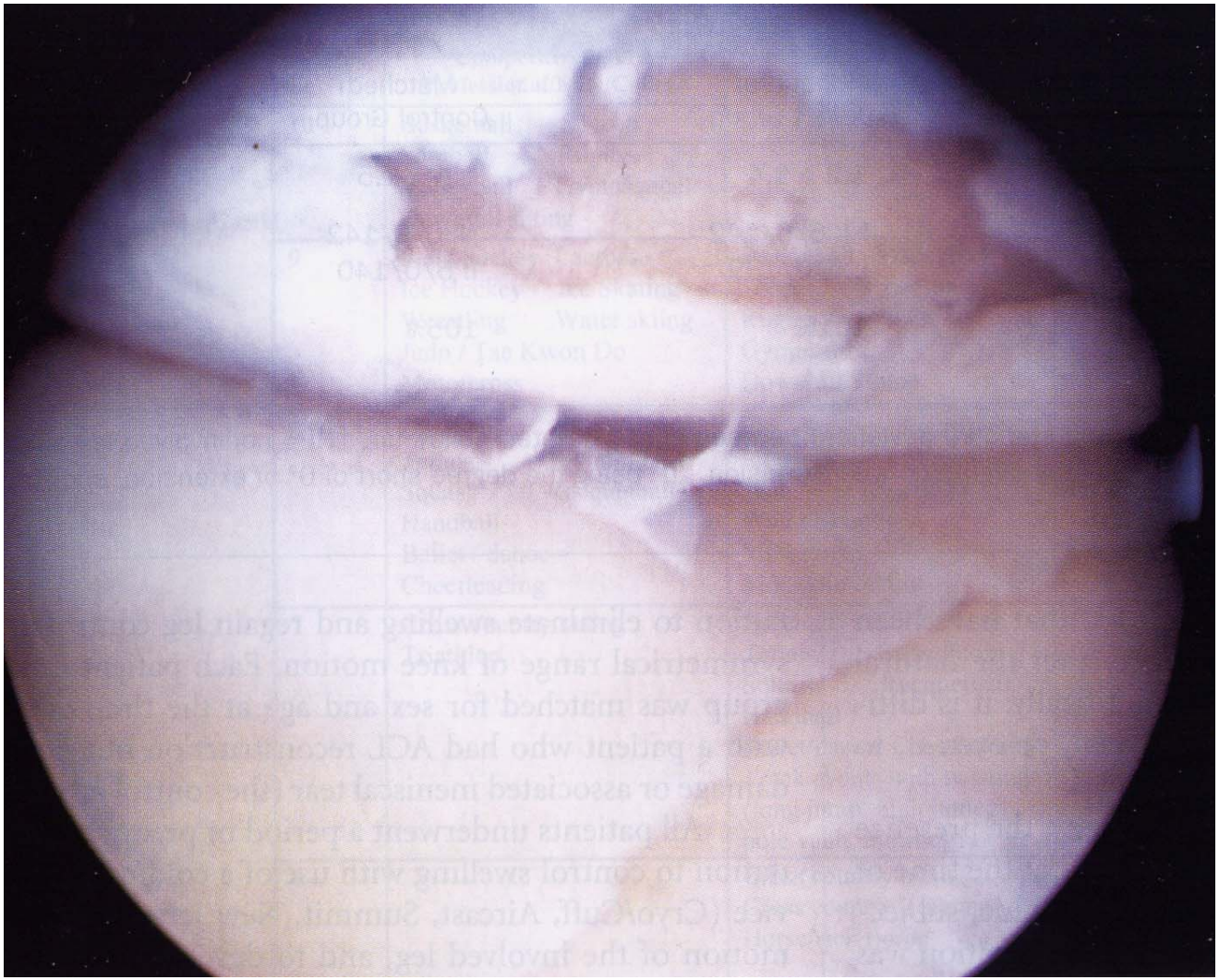
Nuffield Orthopaedic Centre

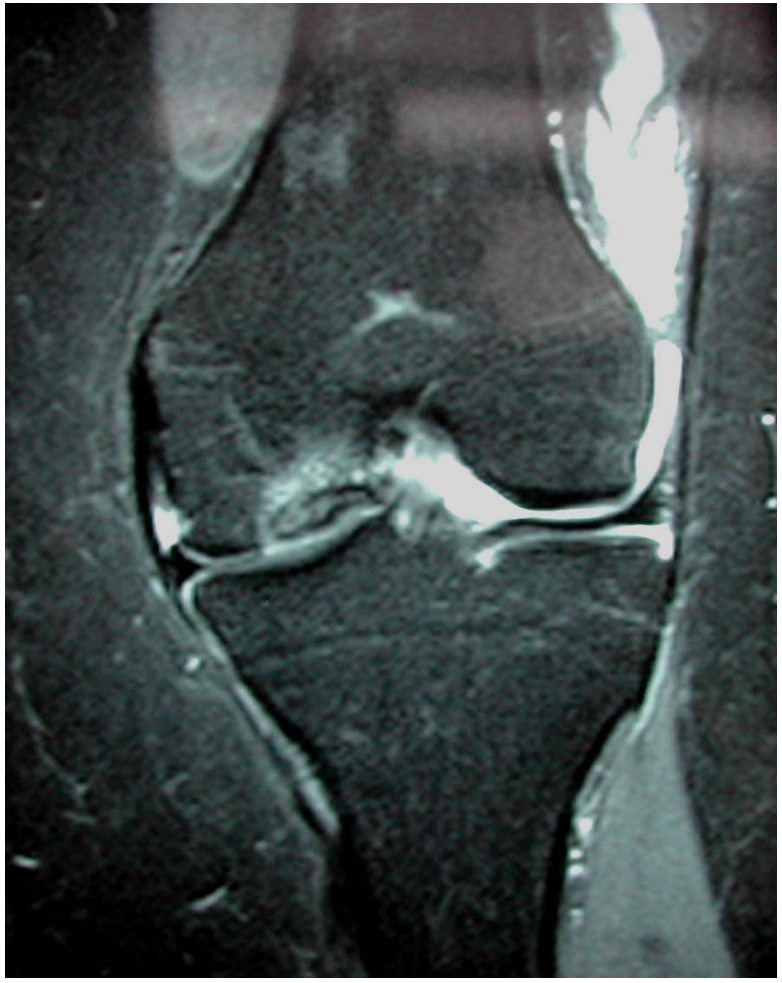





Superficial flattened cells
Vertical rows of cells
Calcified matrix
Bone


Articular surface
Superficial tangential (10–20%)
Middle (40–60%)
Deep (30%)
Calcified cartilage
Tangential fibres
Radial fibres
Perpendicular fibres
Tidemark
Subchondral bone
Cancellous bone





Repair / Regeneration

- Repair
  - New tissue but does not duplicate original tissue
- Regeneration
  - New tissue which duplicates normal cartilage

Repair / Regeneration

- Repair
  - New tissue but does not duplicate original tissue
- Regeneration
  - New tissue which duplicates normal cartilage

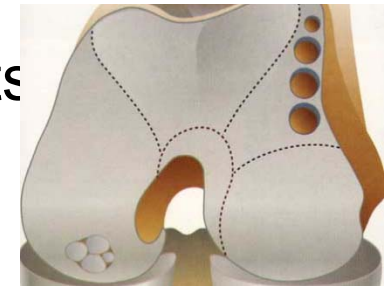
Repair / Regeneration

- Repair — Fibrocartilage
  - Occurs when the subchondral bone plate is breached
- Regeneration — Does not occur

Cartilage Repair

Marrow stimulation techniques
(Microfracture)

Osteochondral grafts
(OATS)



Autologous Chondrocyte Implantation

Autologous Chondrocyte Implantation

- Lars Peterson technique - 1987

- Brittberg et al. 1994

  ‘Treatment of deep cartilage defects of the knee with autologous chondrocyte transplantation.’

  New England Journal of Medicine

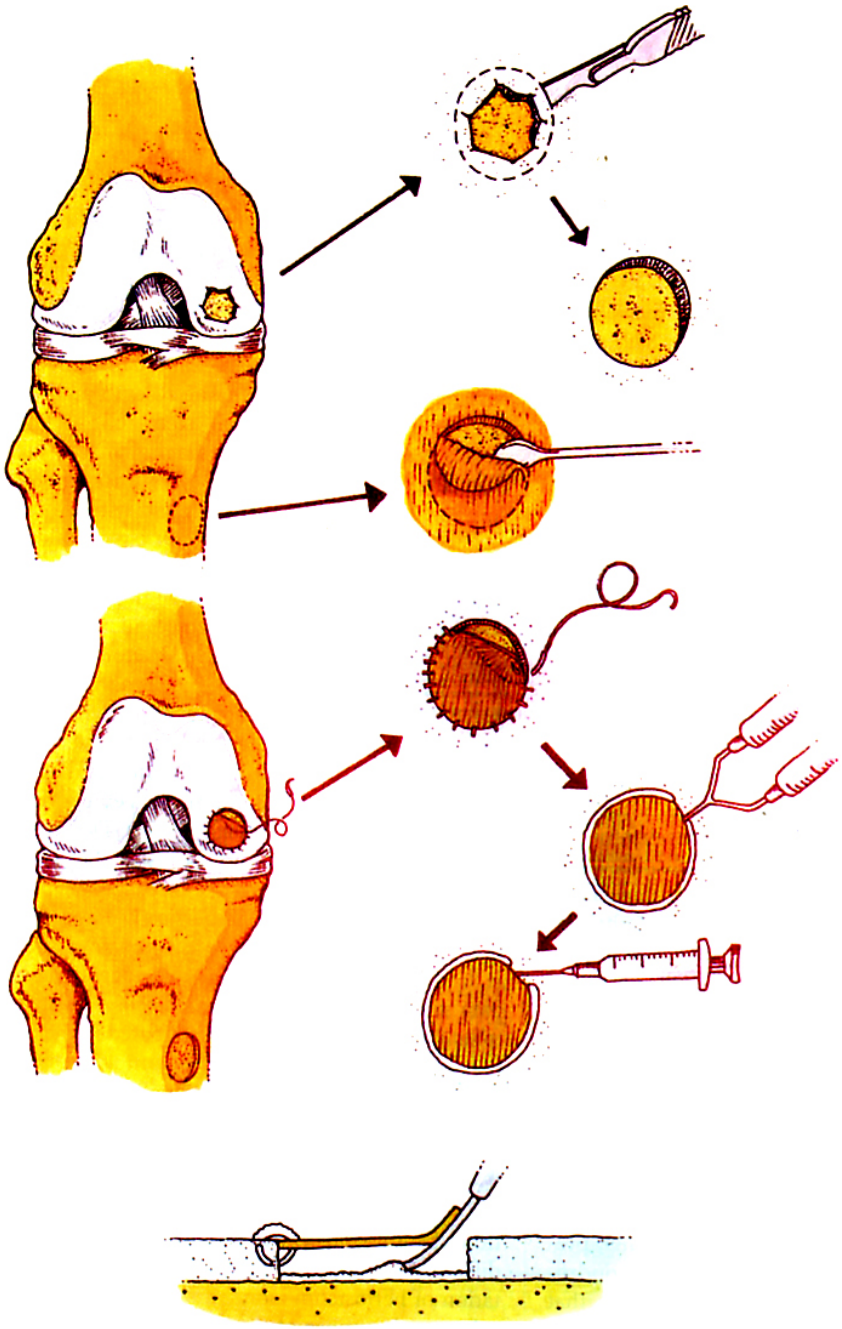
ACI-P

Autologous

Chondrocyte

Implantation

Periosteum



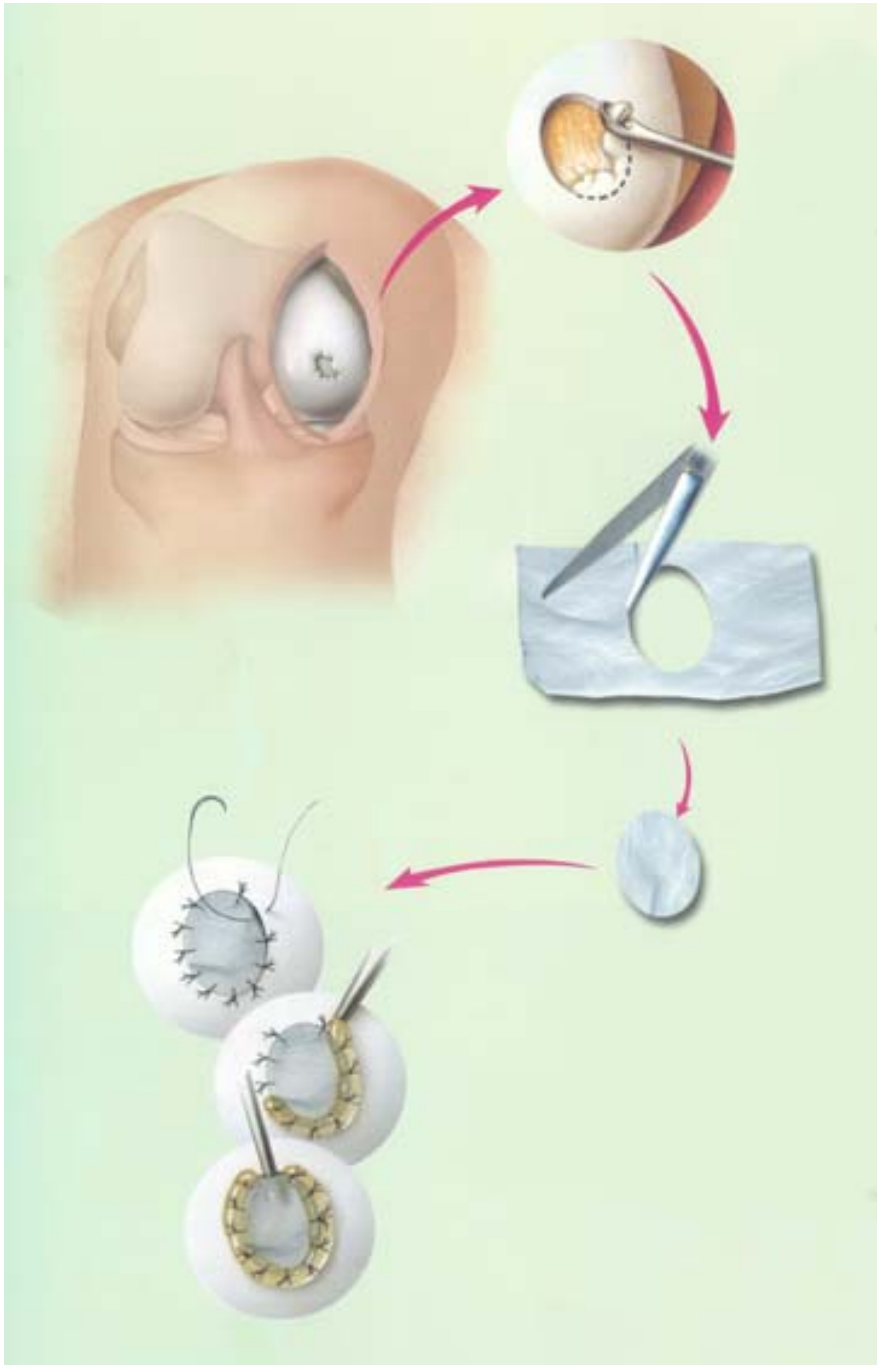
ACI-C

Autologous

Chondrocyte

Implantation

Collagen matrix



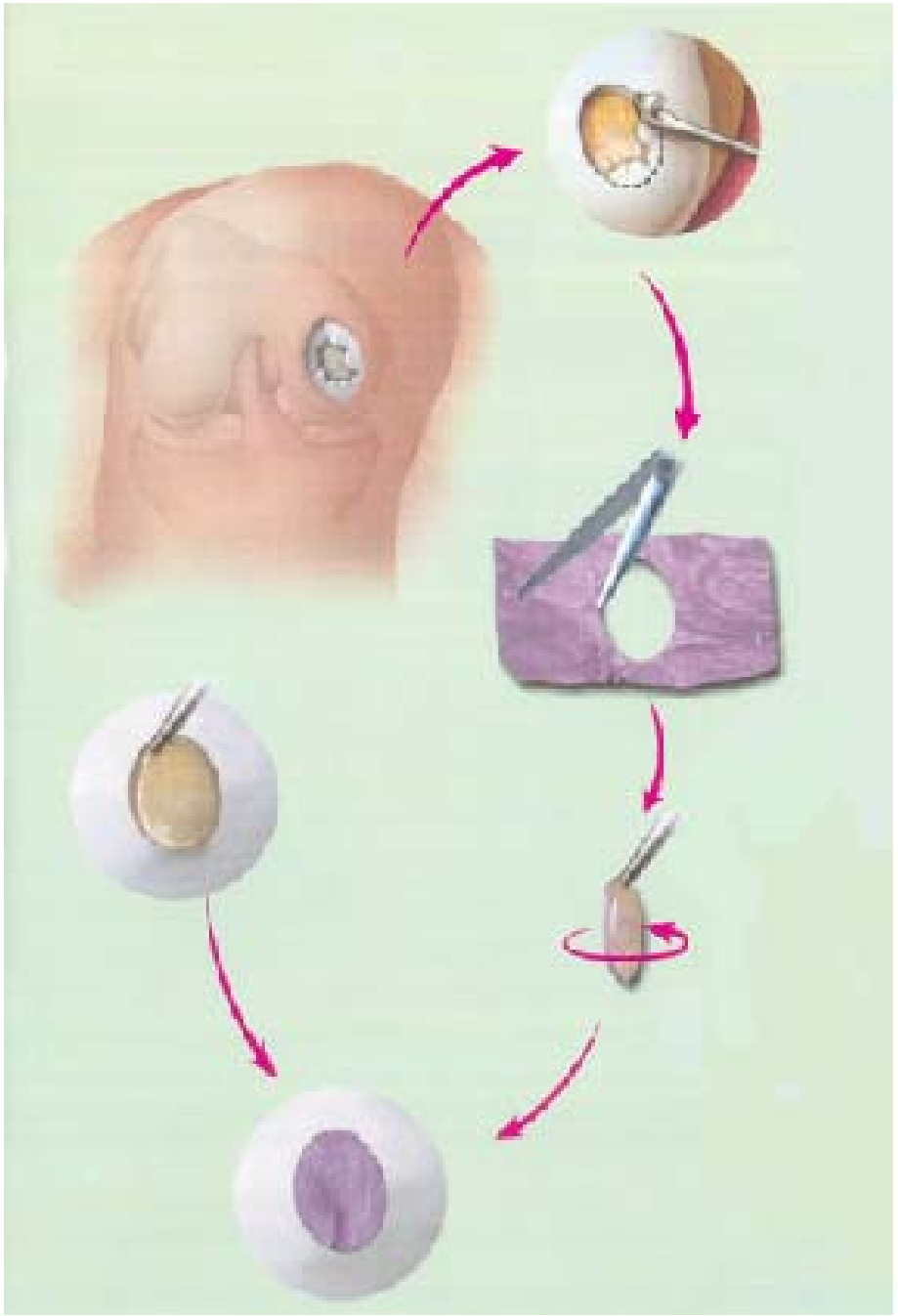
MACI

Matrix induced

Autologous

Chondrocyte

Implantation



ACI Results

- Peterson et al. 2002
  - Up to 11 years post operation
  - 80% of patients maintained improvement
- Other series with shorter follow-up
  - Micheli et al. 2001
  - Gillogly et al. 1998
  - Minas 2001

RCTs

- Horas et al. 2003
  - Mosaicplasty > ACI
- Bentley et al. 2003
  - ACI > Mosaicplasty
- Knutsen et al. 2004 & 2007
  - Microfracture = ACI

NICE

ACI review: Further research required

Second line treatment

Cases should be entered into trials

Autologous Chondrocyte Implantation

- Numerous cohort studies with good clinical results
- 10 year studies suggest benefits are lasting
- Prevents/slows early arthroplasty
- In comparison to other cartilage repair methods it does at least as well.
- Better at treating larger defects than alternatives

Introducing ACI to the NOC

Developing a cartilage repair service

- Part of the range of procedures required
- Salvage cases
- Surgeon trained in the field

NICE Technology Appraisal 16

‘The use of ACI for the treatment of cartilage defects in knee joints’

- Not recommended for the treatment of cartilage lesions
- If used patients must be entered into clinical trials
- Patients must be made aware of the uncertainties around the long-term outcome of the method

Introducing ACI to the NOC

Meeting NICE guidelines

- Stanmore Multicentre RCT
- ACI versus MACI

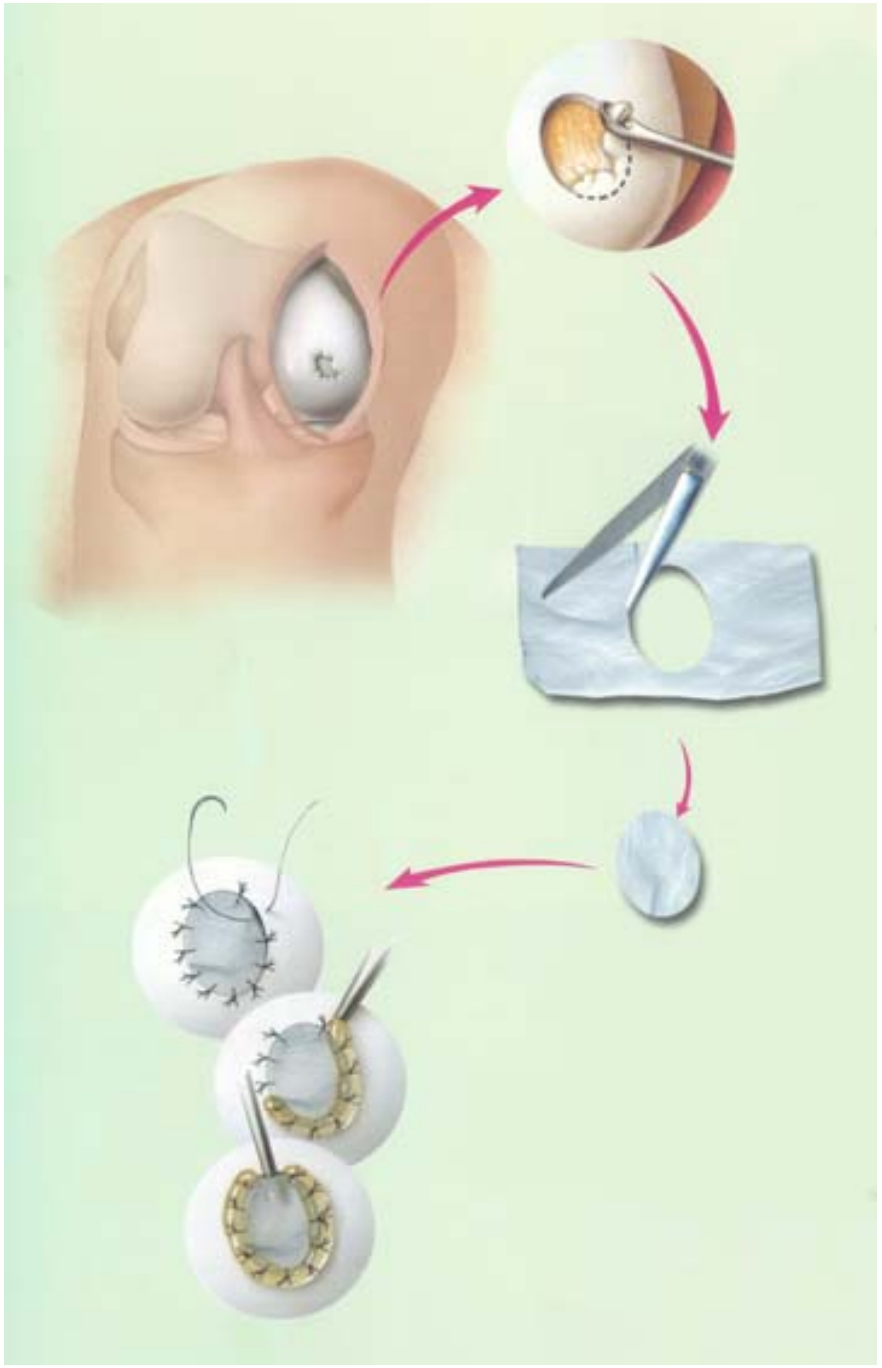
ACI-C

Autologous

Chondrocyte

Implantation

Collagen matrix



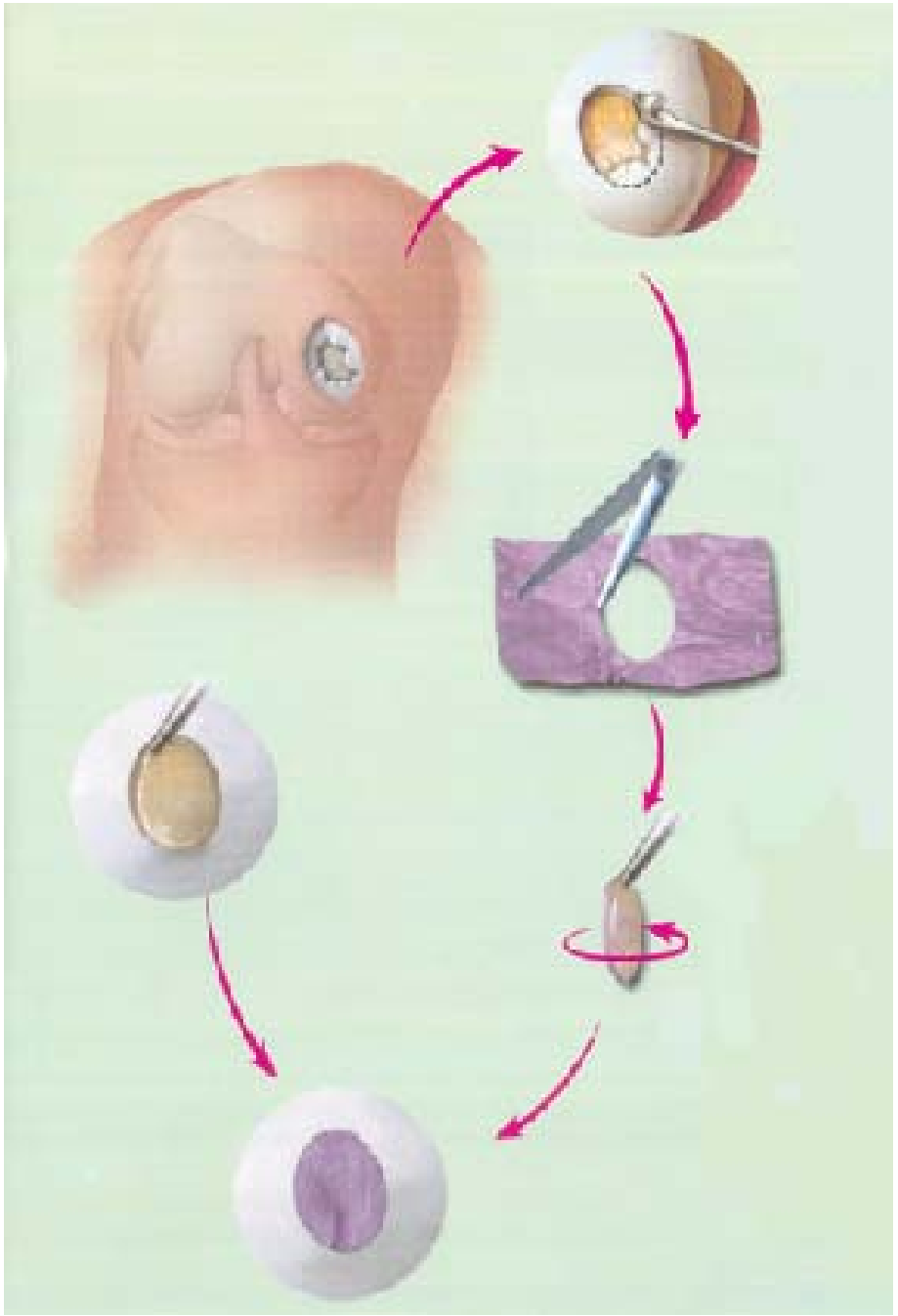
MACI

Matrix induced

Autologous

Chondrocyte

Implantation



ACI at the NOC

20 patients treated

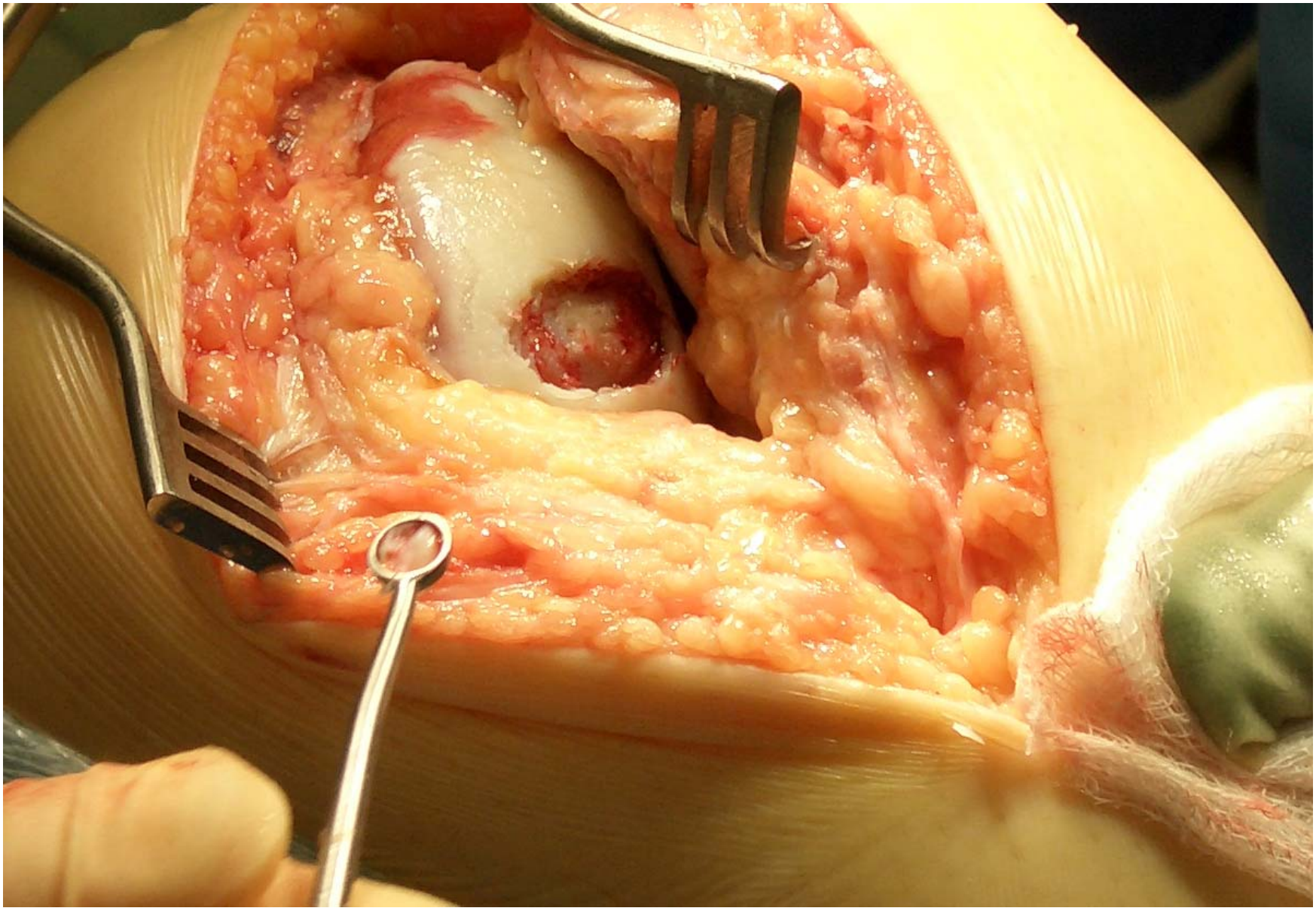
Patients entered into Stanmore Trial

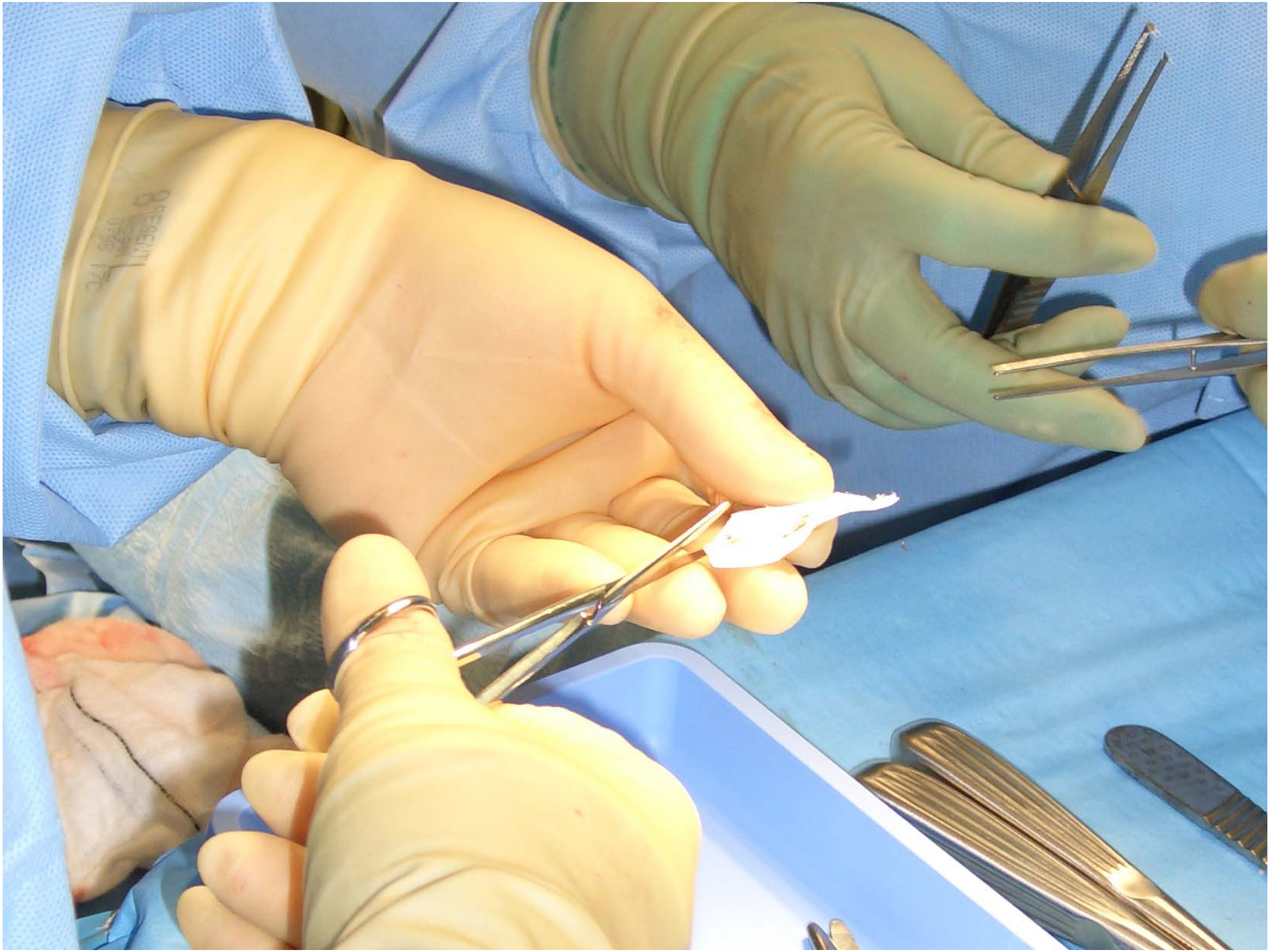
Internal audit of results

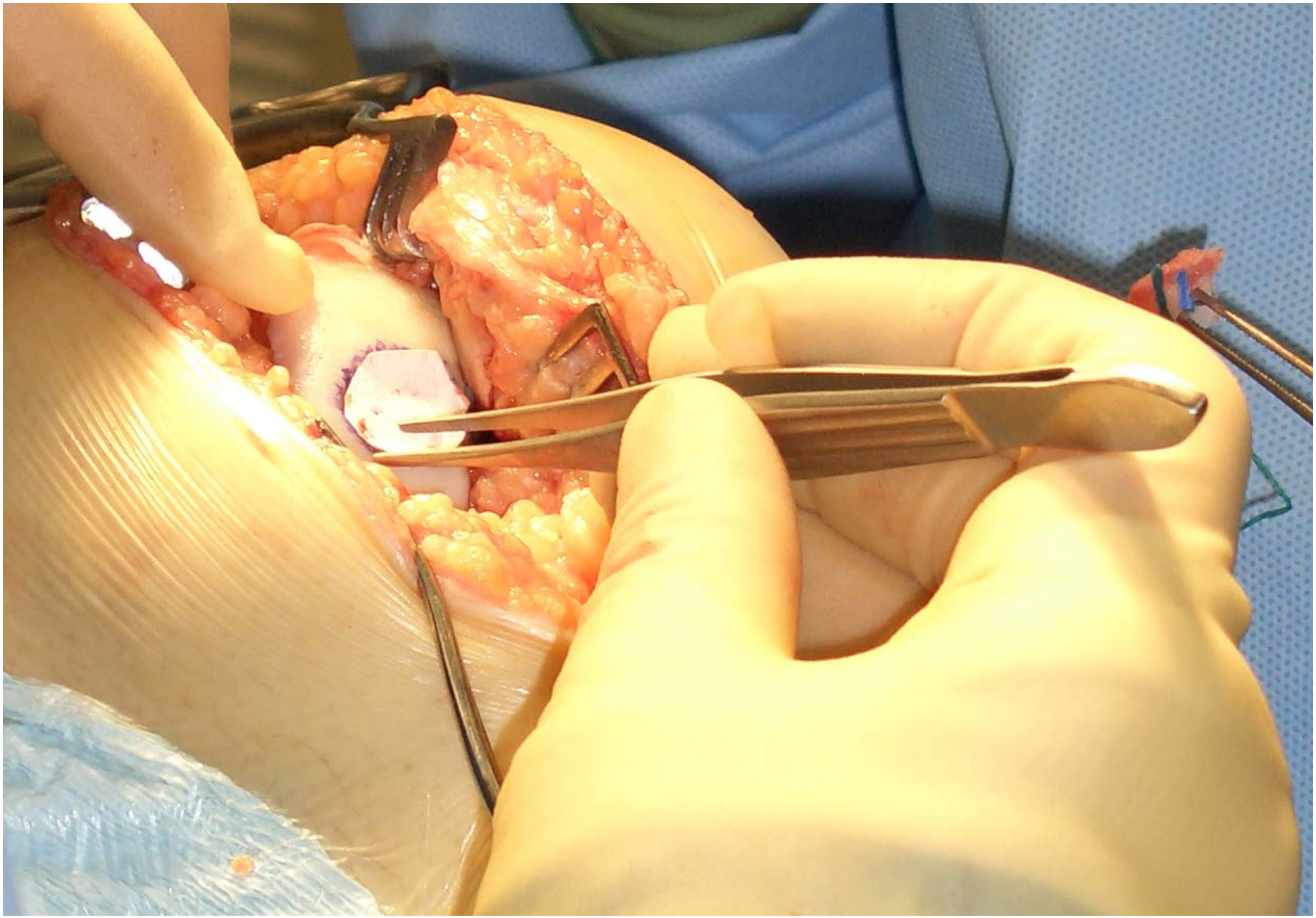
Introducing ACI to the NOC

First case: 20th May 2005

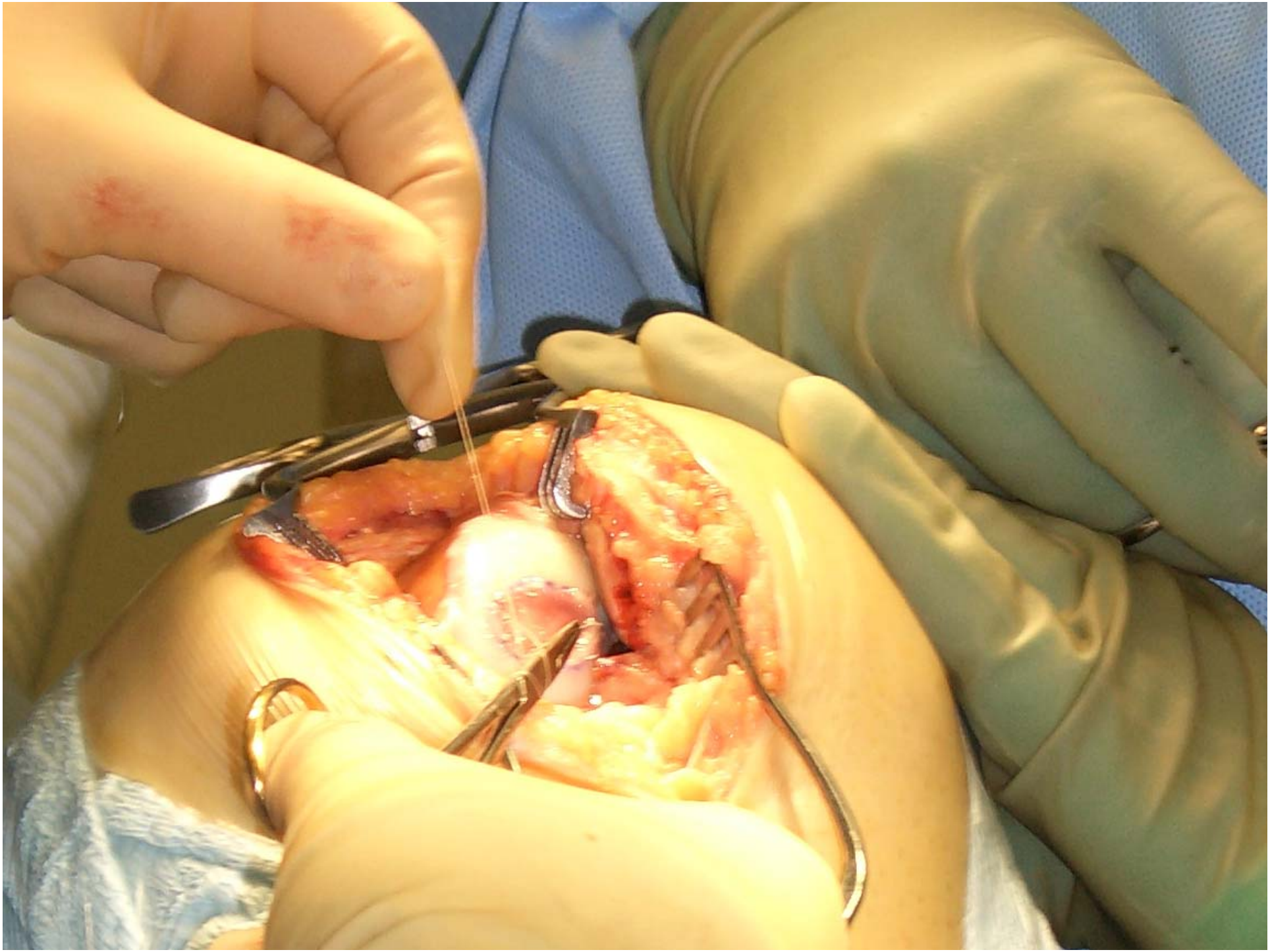
Andrew Price



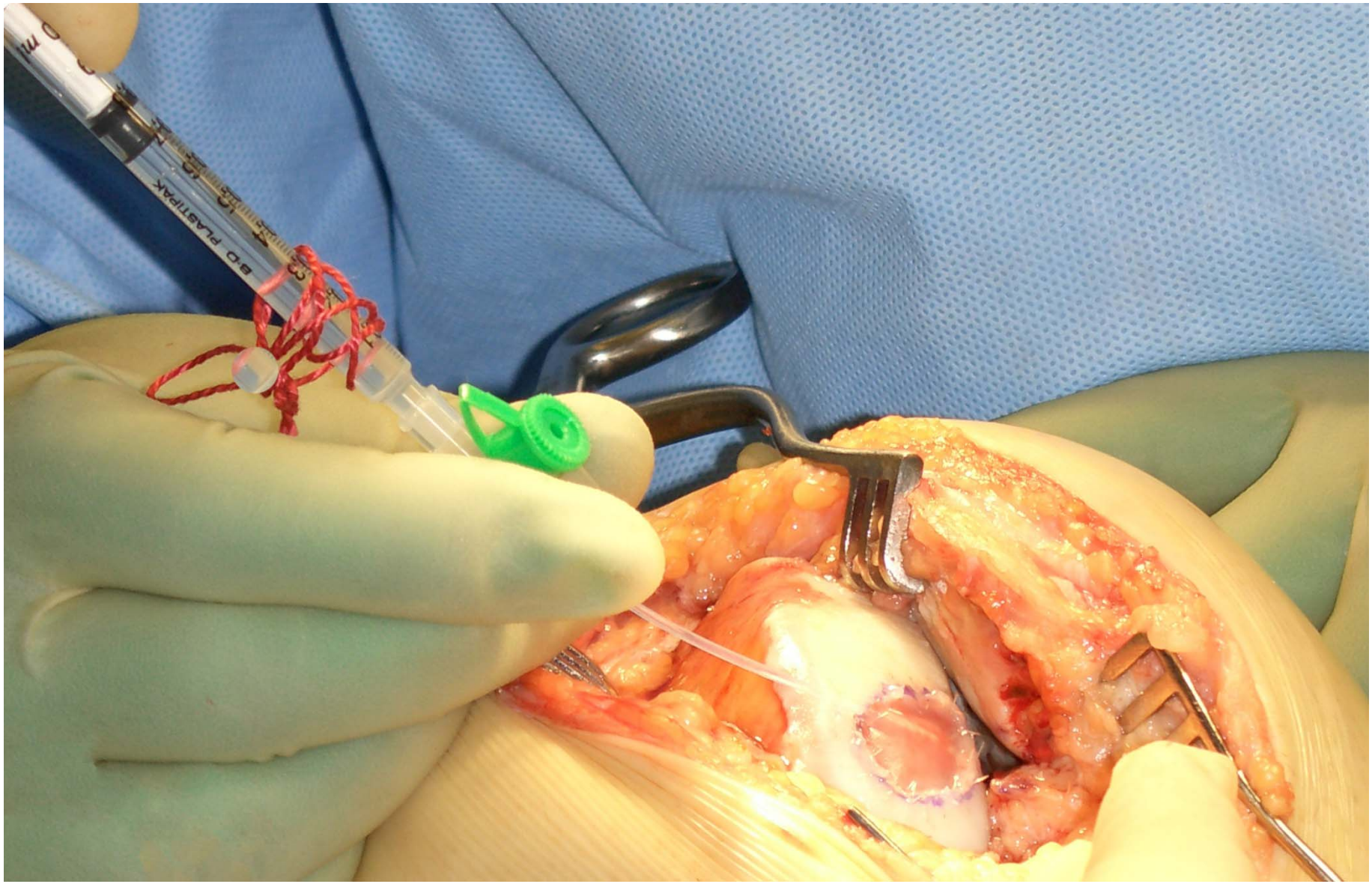


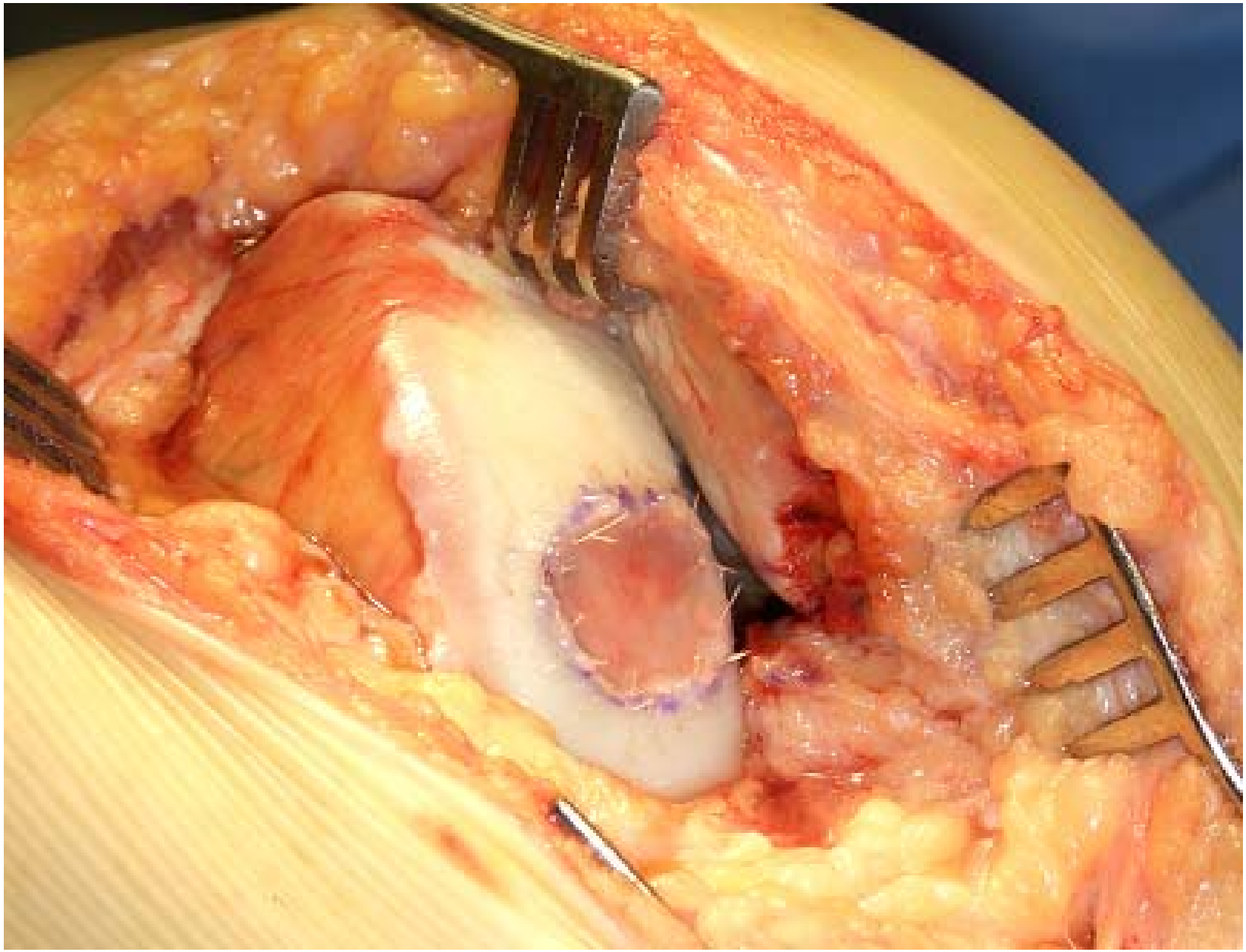



DO NOT FREEZ
STORE AT ROOM TEM
+10°C TO +25°C




20
30
40
50
ml
60
BRAUN
Universal


B-D PLASTIPAK

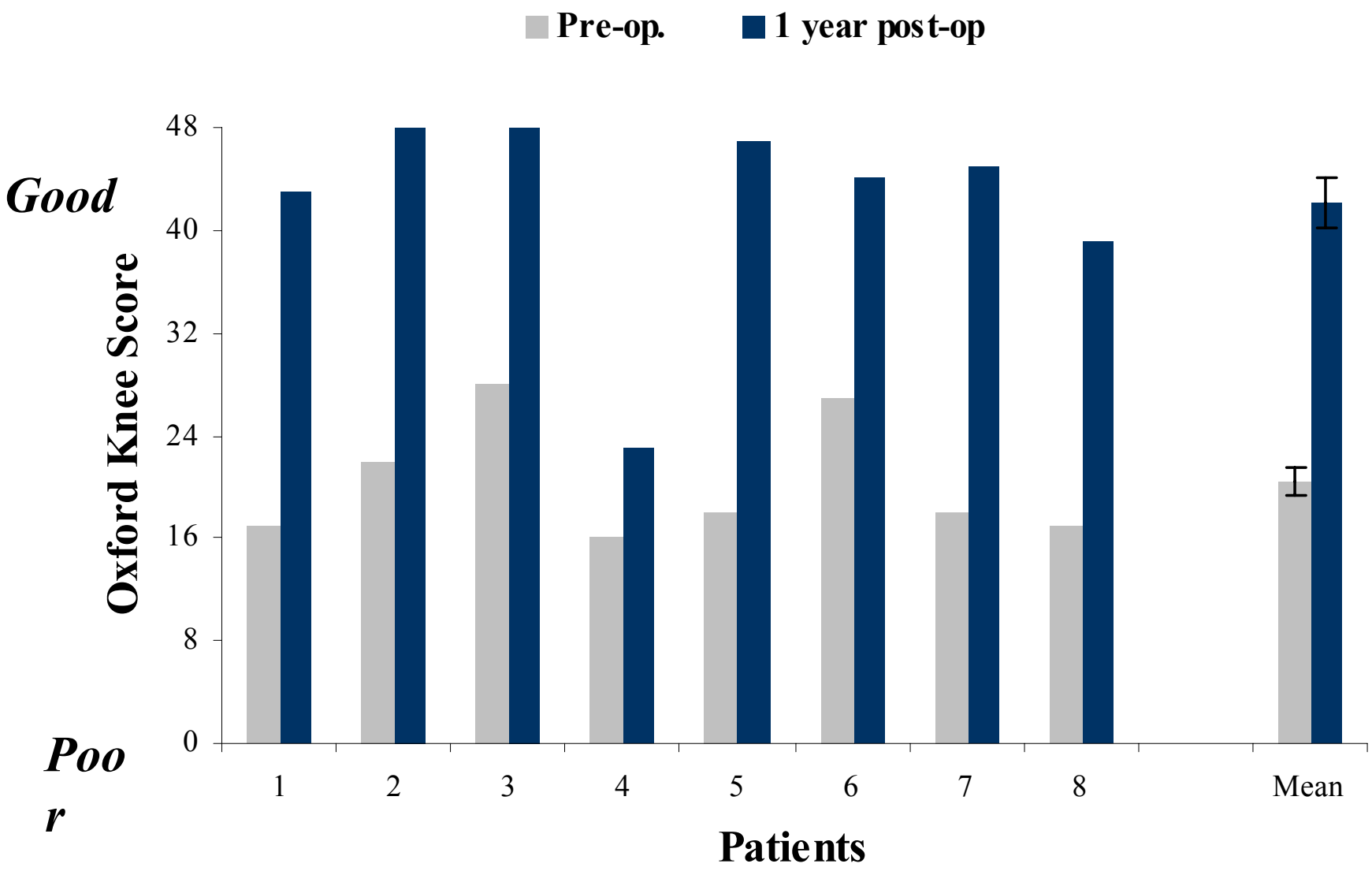


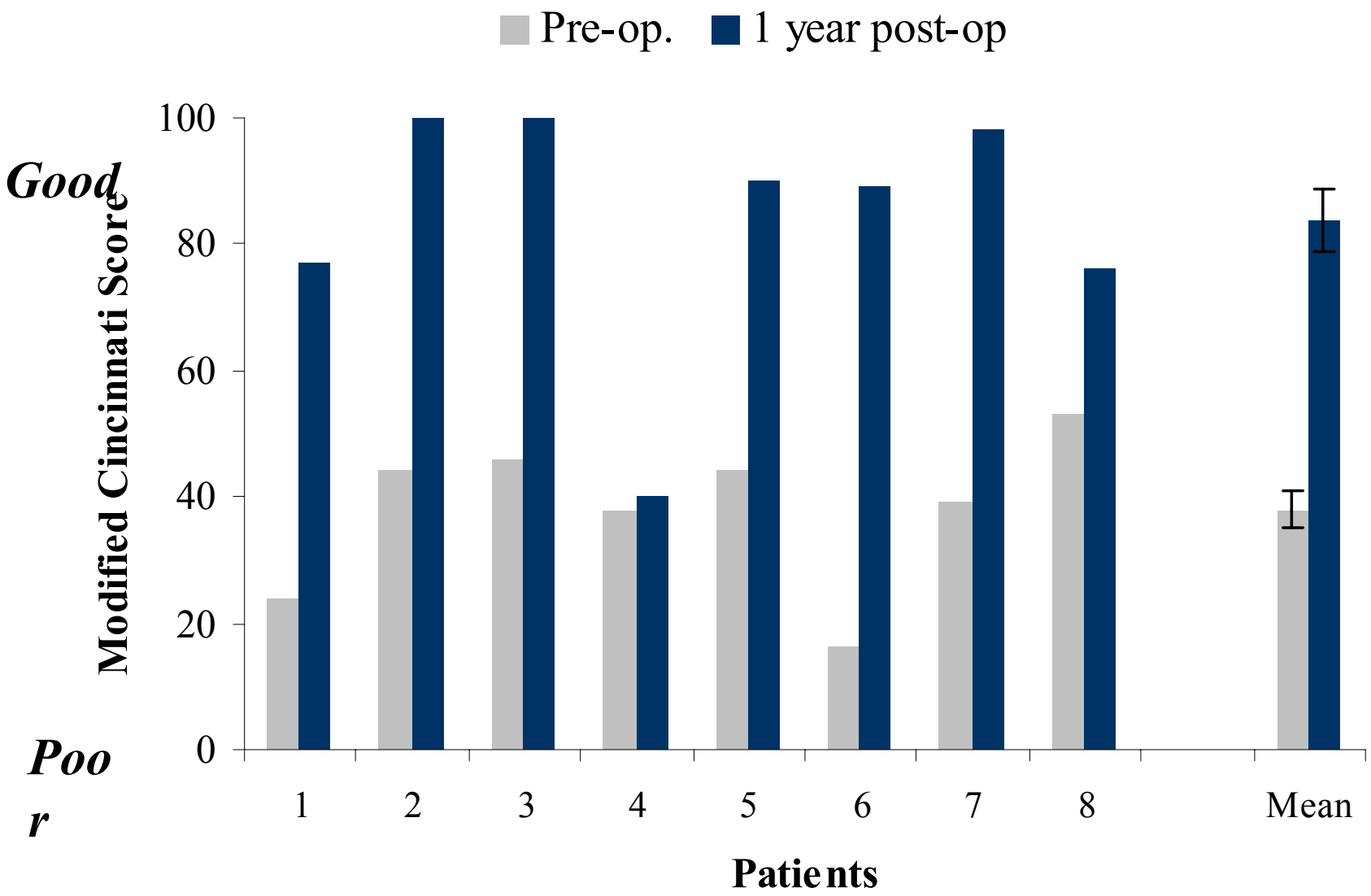
NOC series of ACI

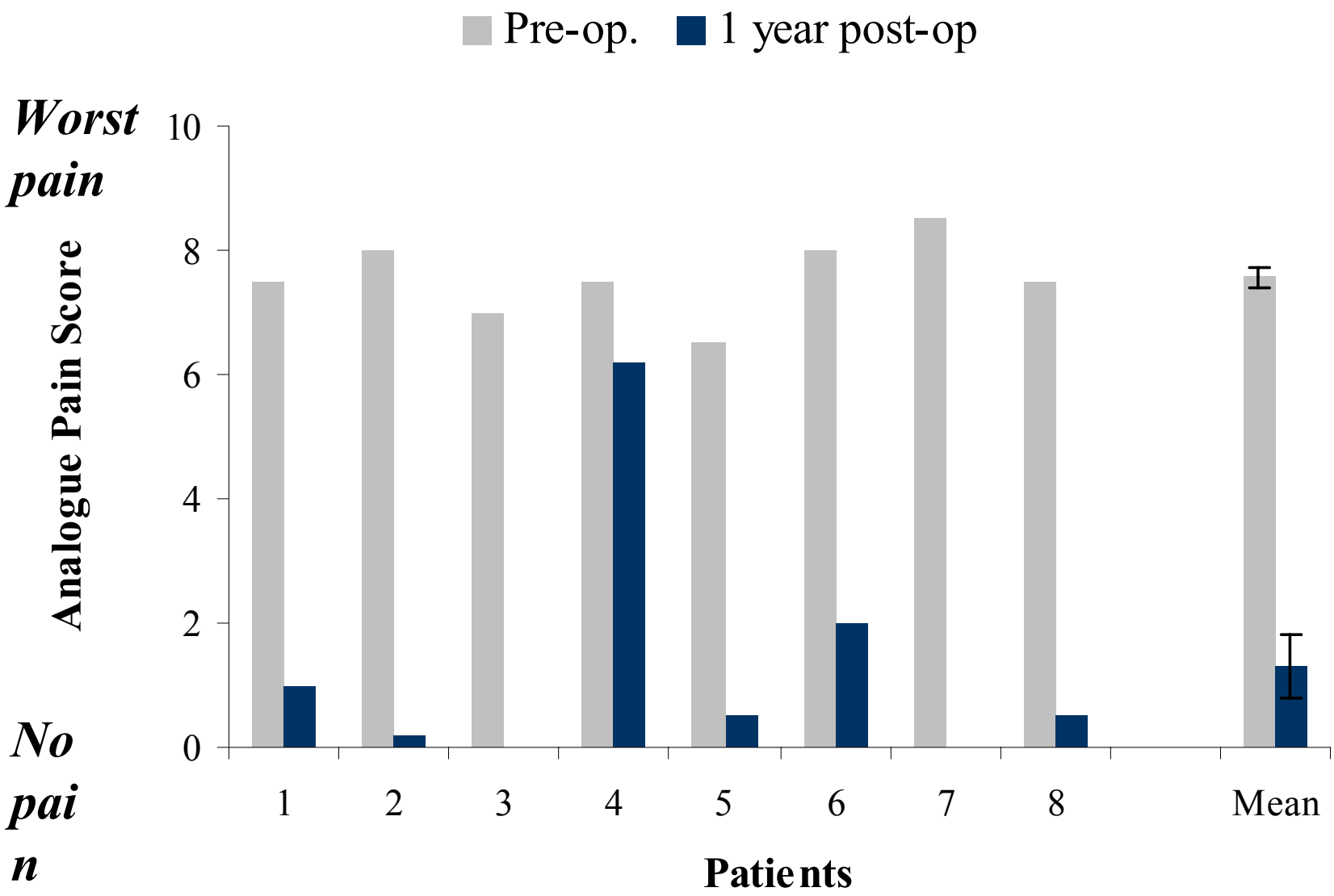
Outcome measures (pre-op, 1 year)

- Oxford Knee Score (0 to 48)
- Modified Cincinnati Score (0 to 100)
- Visual analogue pain score (0 to 10)

- All NOC 8 at one year post-operation


Pre-op.
1 year post-op
Good
Poor
Oxford Knee Score
48
40
32
24
16
8
0
1
2
3
4
5
6
7
8
Mean
Patients


Pre-op.
1 year post-op
Good
Poor
Modified Cincinnati Score
100
80
60
40
20
0
1
2
3
4
5
6
7
8
Mean
Patients


Pre-op.
1 year post-op
Worst pain
No pain
Analogue Pain Score
10
8
6
4
2
0
1
2
3
4
5
6
7
8
Mean
Patients

NOC series of ACI

Summary

- 7 successful procedures
- 1 failure
- Encouraging clinical results in salvage group

ACI, NOC & NICE

What next?

- Caution in ACI's use remains vital
- Appears to be a valuable clinical intervention
- True indications need to be identified

Questions

- Durable?
- Kissing defects?
- Confounding factors?

Treating early OA

Treating early OA

- ? Application of ACI
- Age range in reported series of ACI 30-50.

ACI application in OA

Dr Tom Minas MD

Brigham and Women's Hospital
Boston
USA

Mr David Wood

Perth, Australia

- Extended indication for ACI
- Early OA medial compartment
- Correctable varus deformity
- Full thickness femoral lesions
- No full thickness tibial lesions


S
Pert

HTO + MACI

HTO + MACI

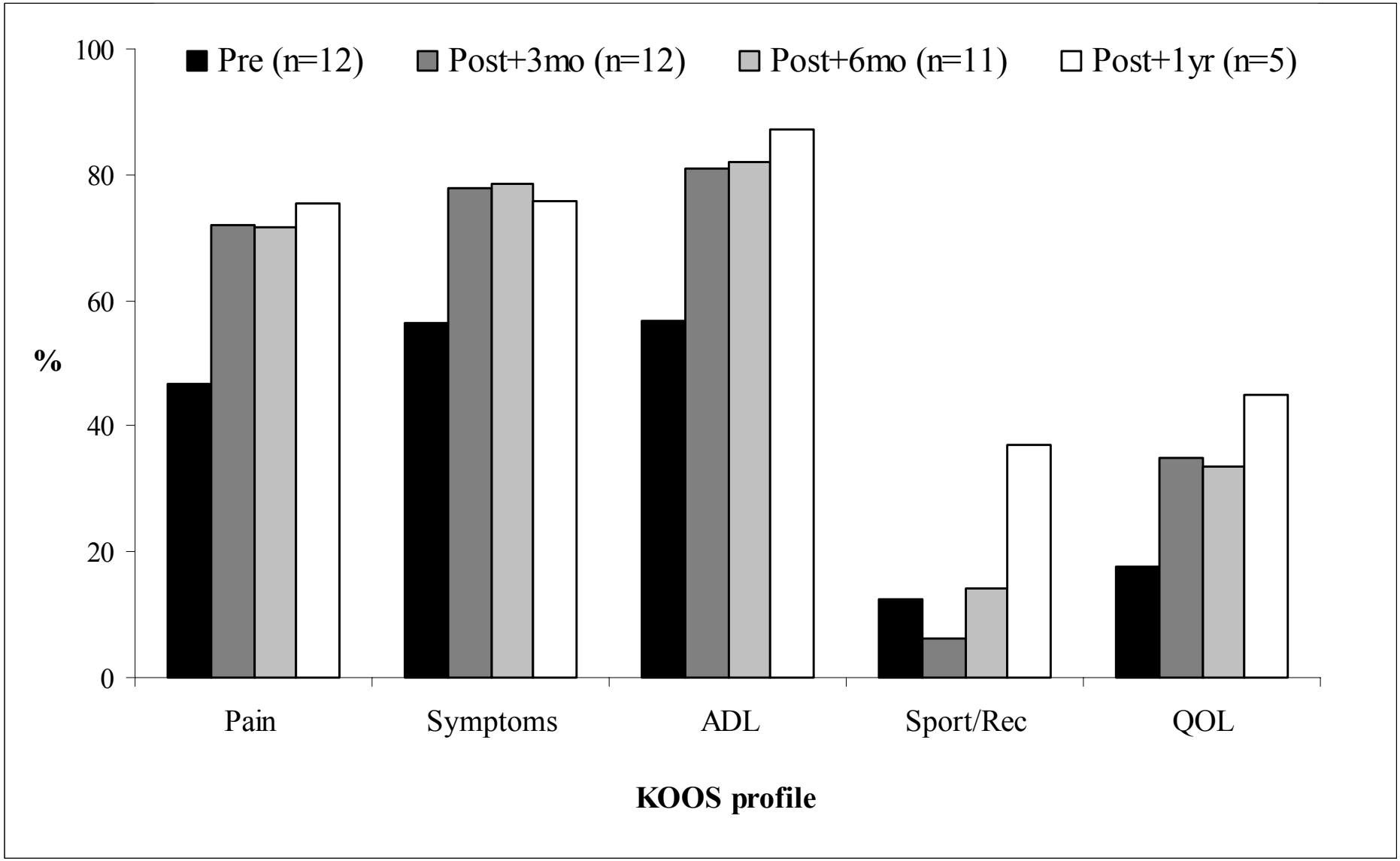
MACI & HTO
(n=12)

Mean age: 47yrs (27 – 58yrs)

Average varus deformity: 6°

Average graft: 5.9cm^2

Early Functional Outcome



MRI results

- Defect in-fill
- Mean graft thickness
  - 0 mm pre-op
  - 1.5 mm at 3 months
  - 2.0 mm at 12 months

Dr Tom Minas

Boston, USA

- Using ACI for salvage in early OA
- Patients too young for TKA (30-50)
- Early OA
  - 50% loss of joint height
  - Peripheral osteophytes
  - Bipolar kissing lesions

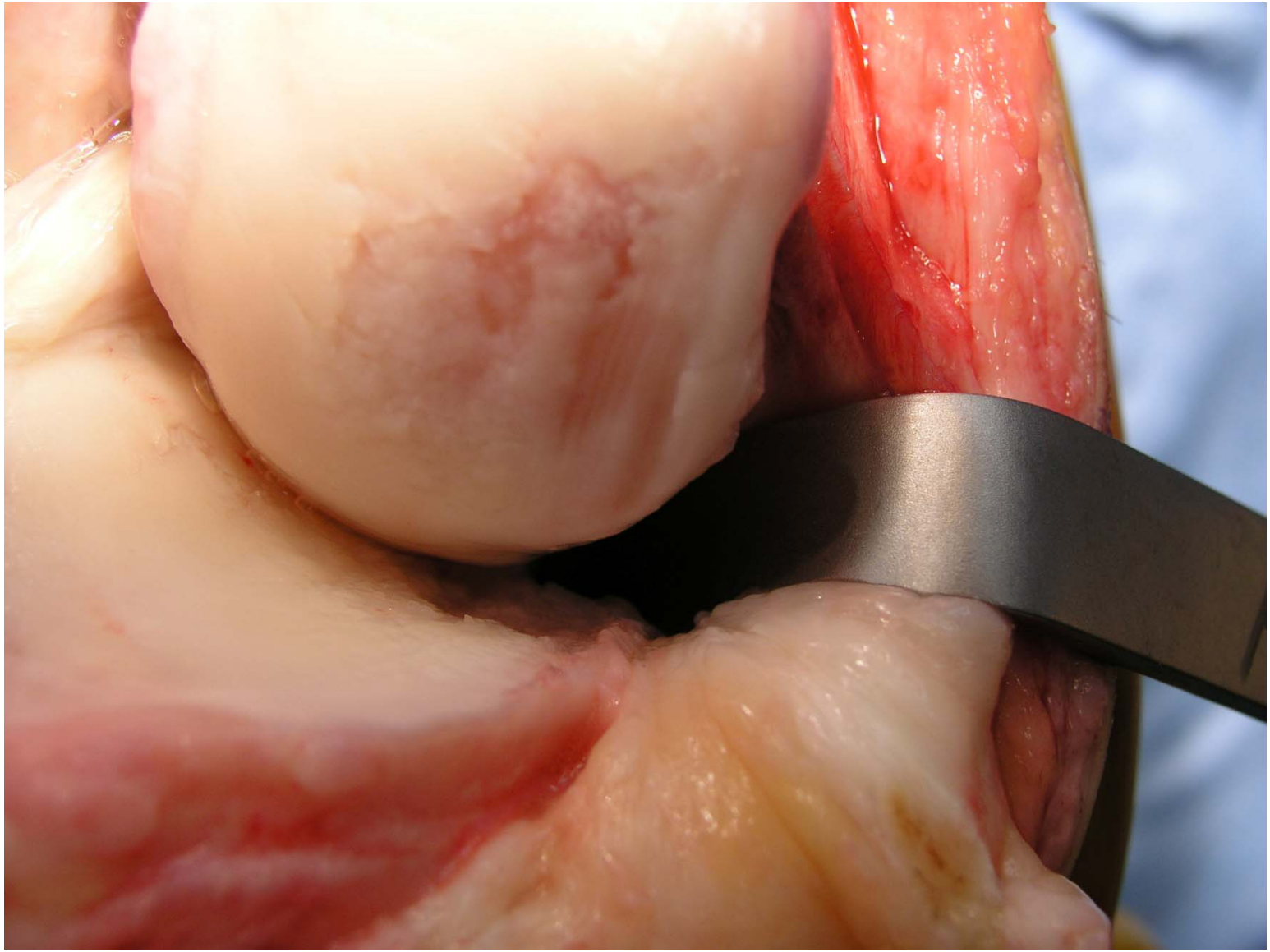
Dr Tom Minas

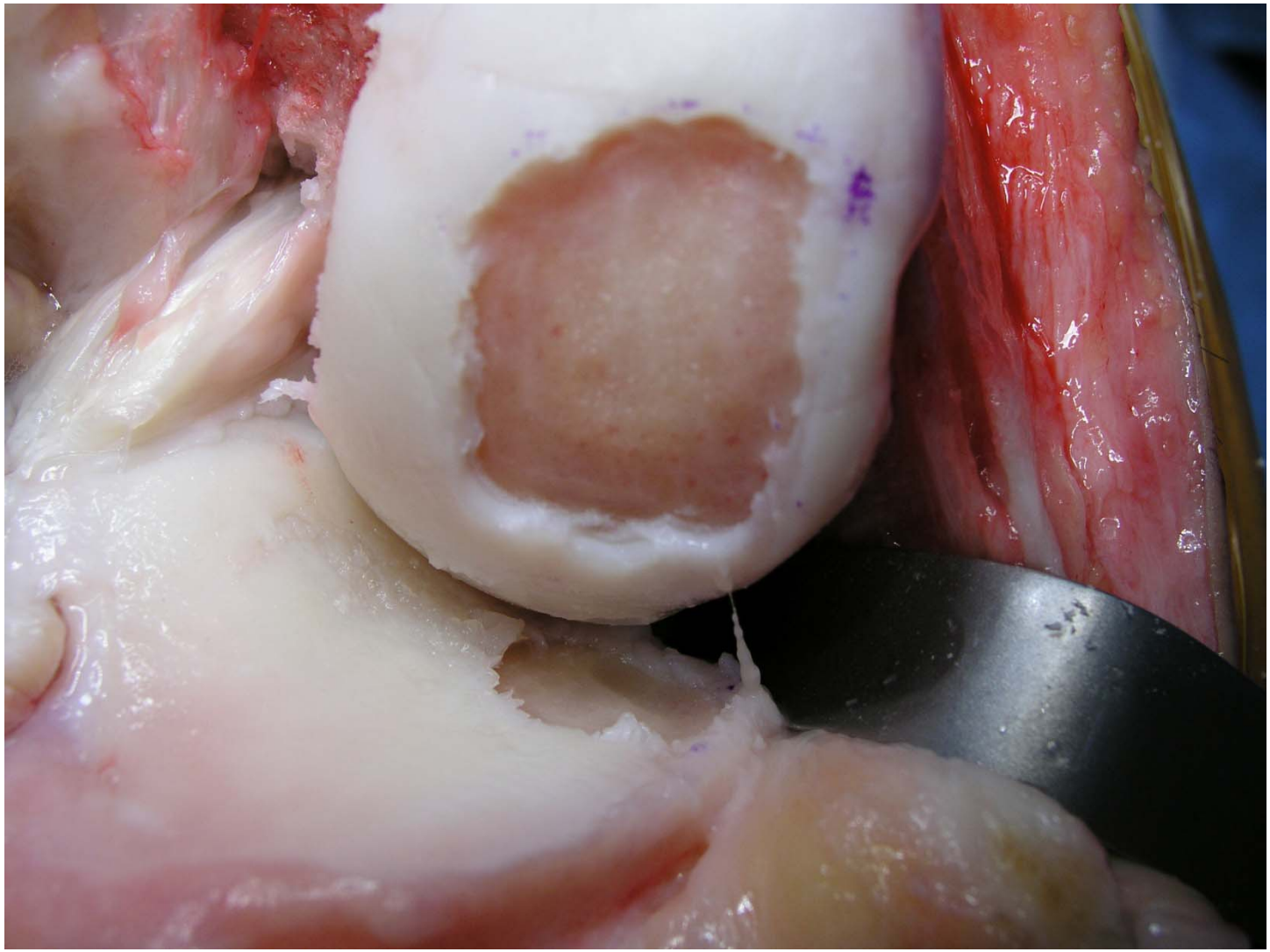
Boston, USA

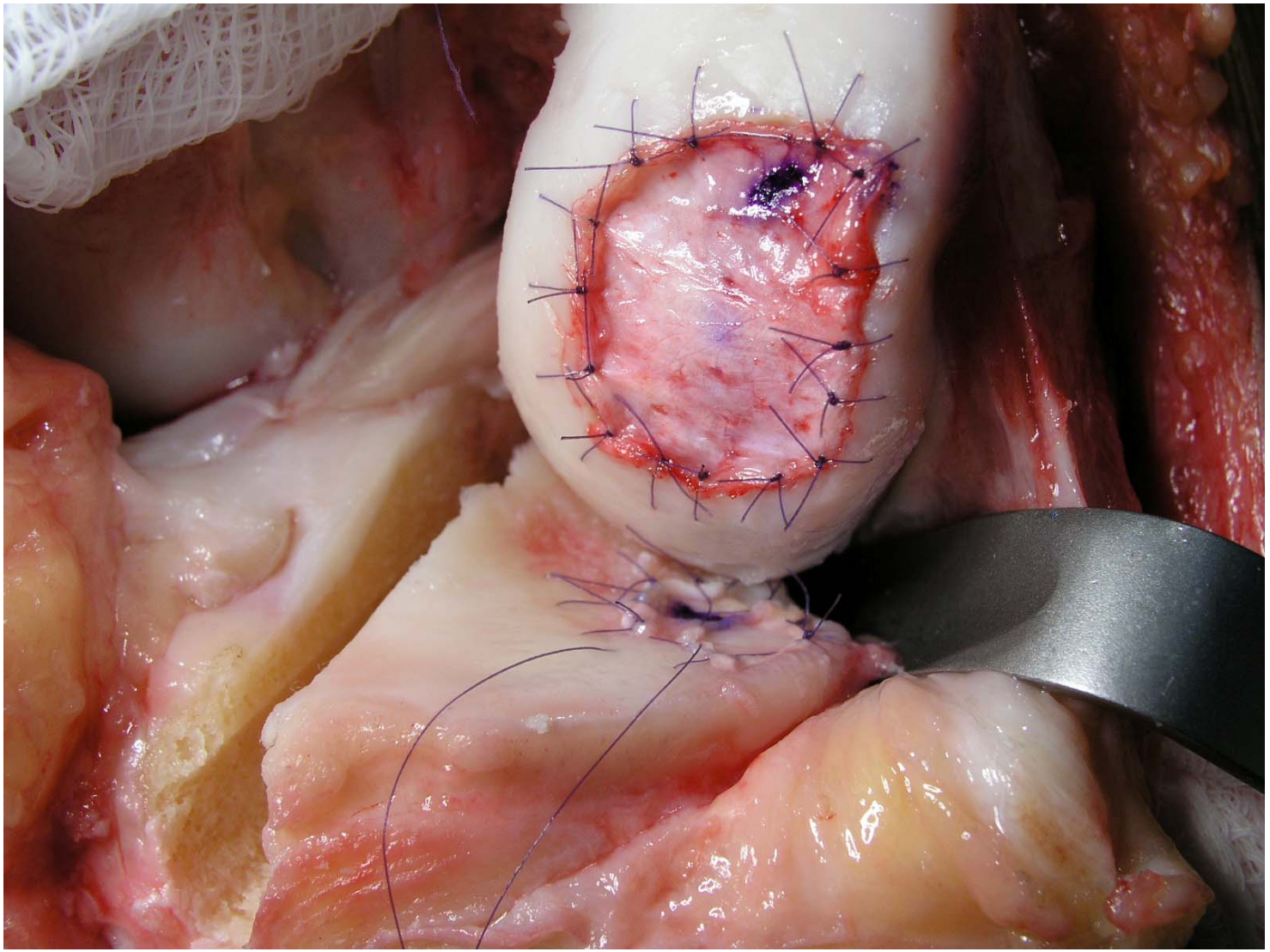
- Biological repair
- ACI-P
- Augmented with other procedures
  - HTO
  - TTO
  - Meniscal allograft
  - ACL reconstruction

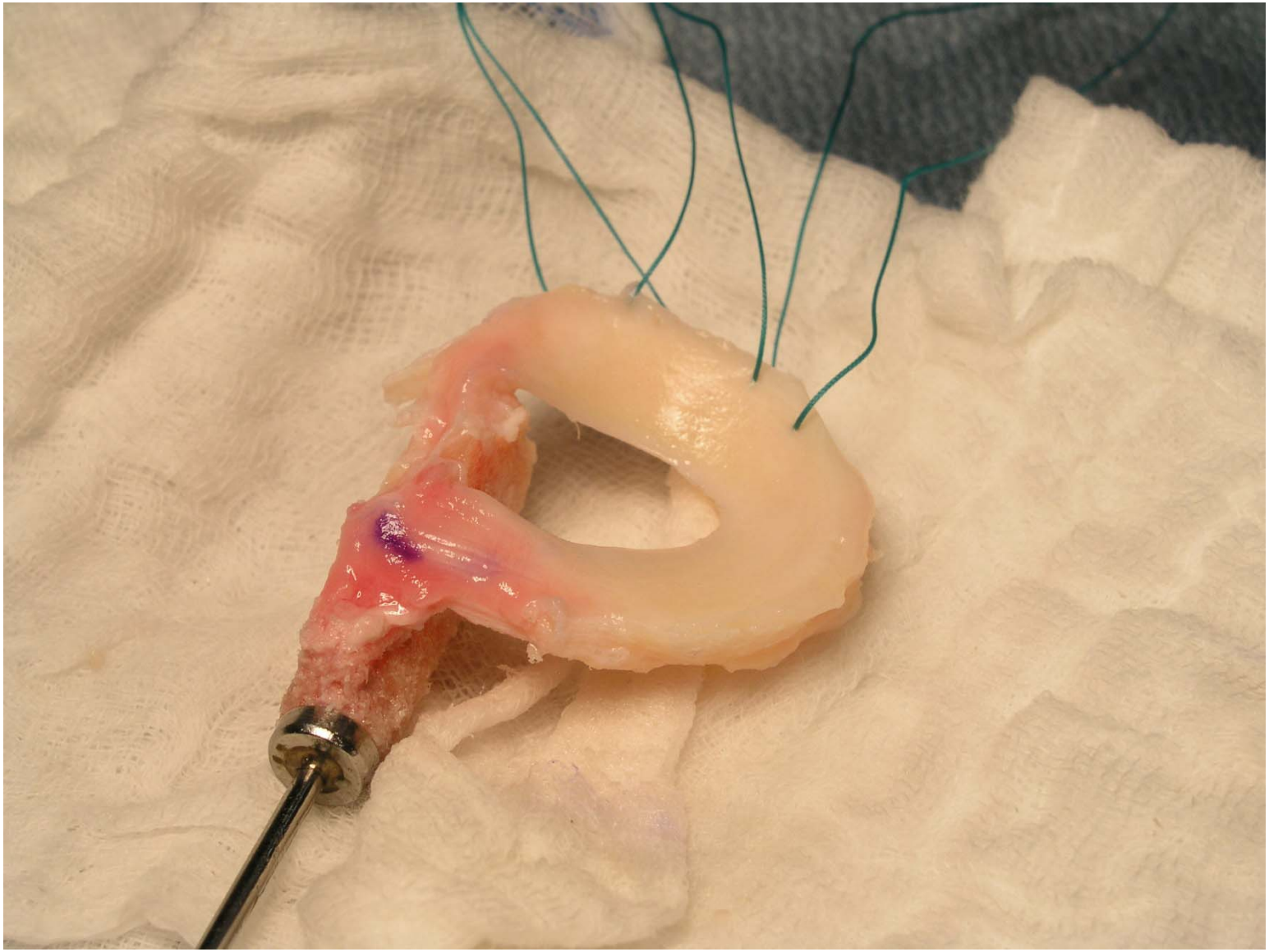
Case 1

- 38 female





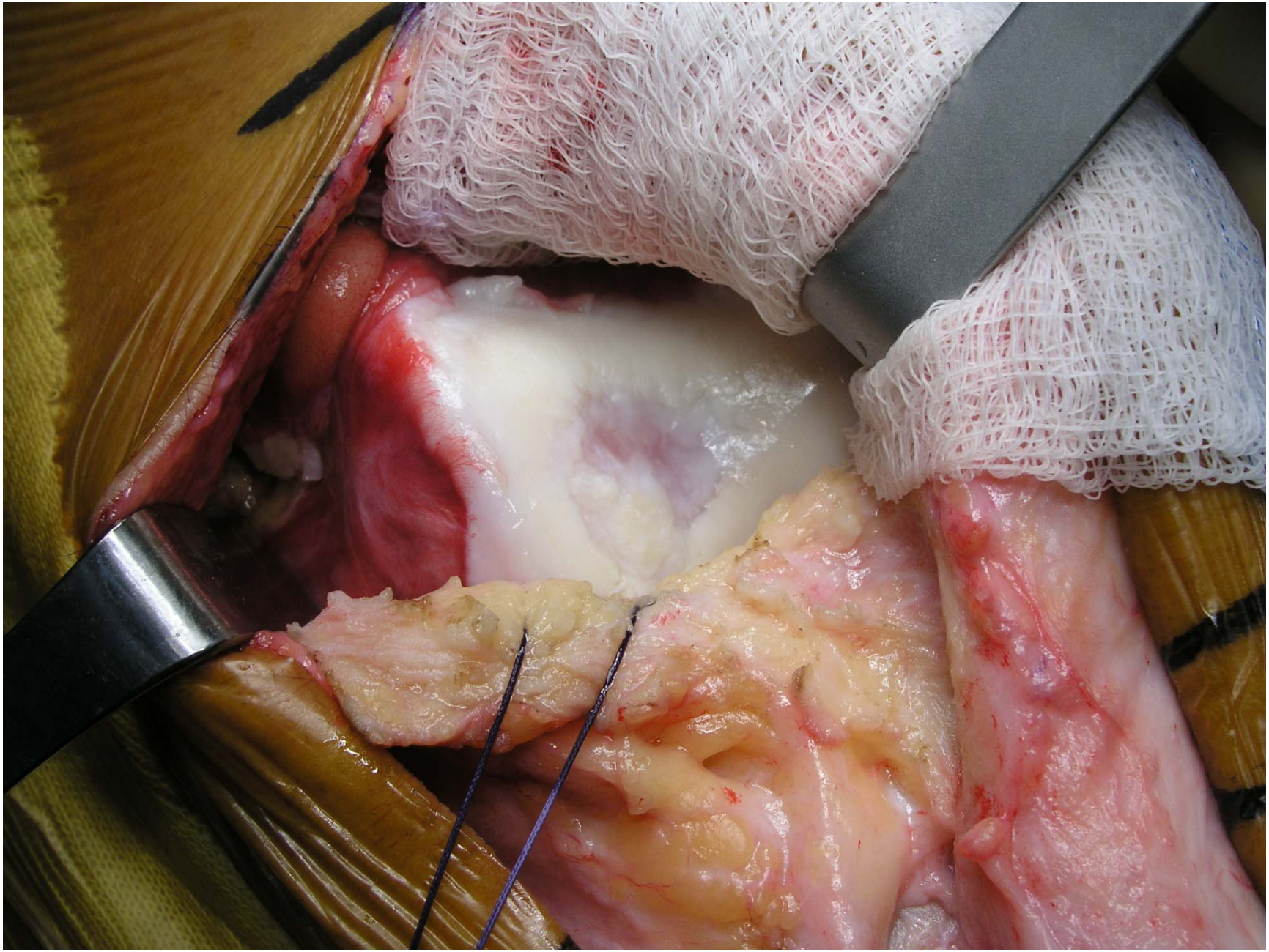


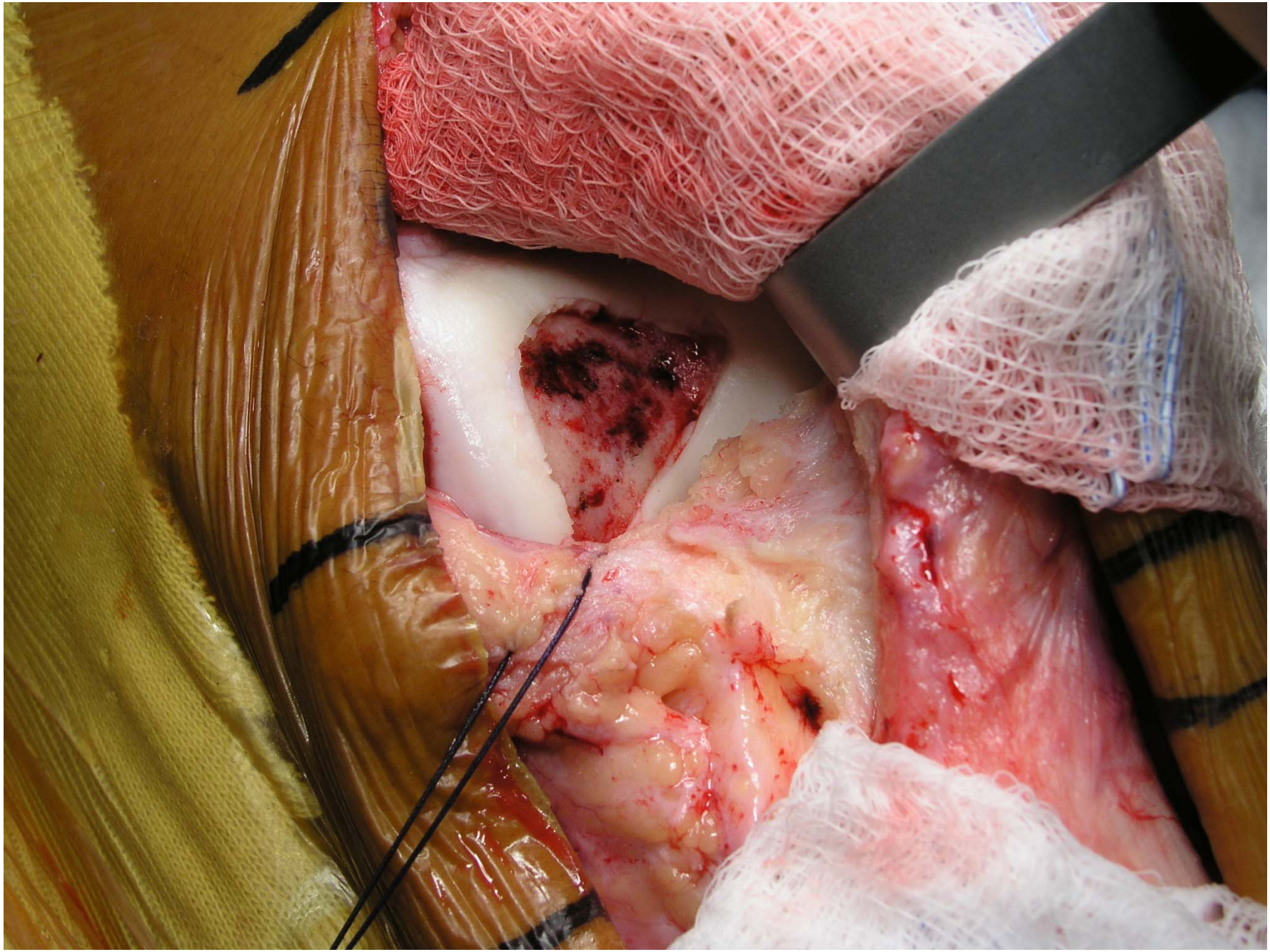


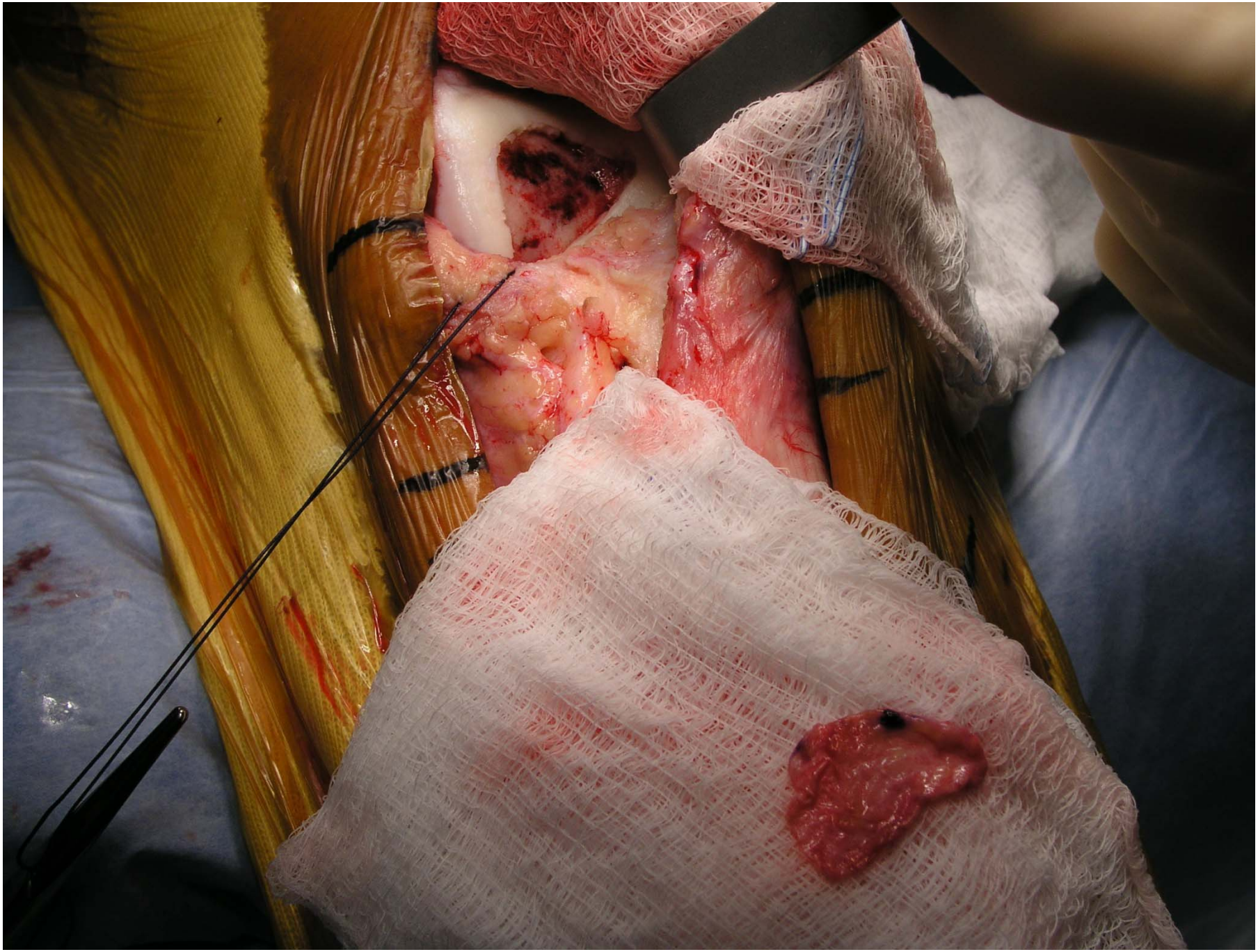
Case 2

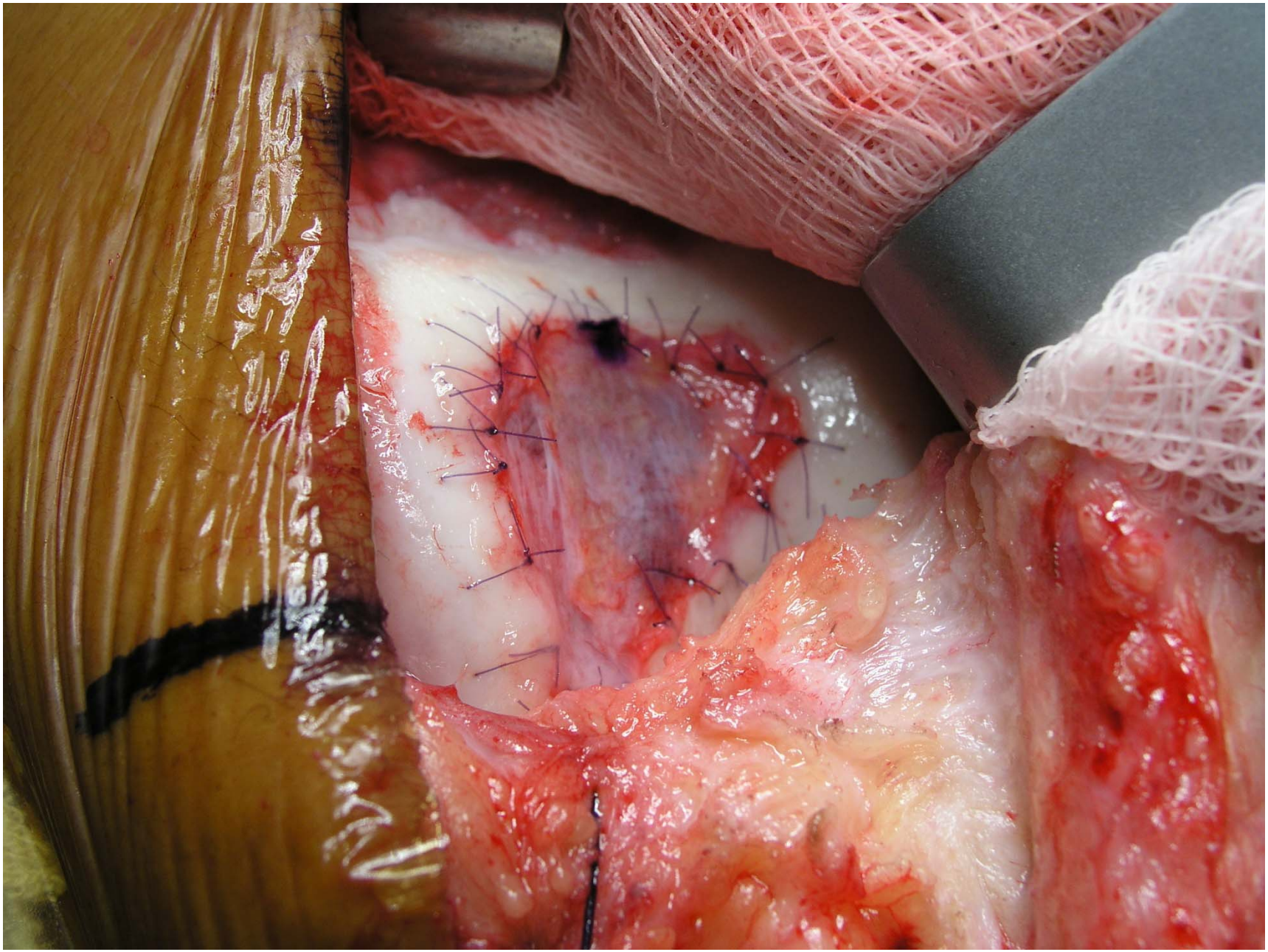
- 42 female


[AR]
[PL]
[F]
C886
W1772



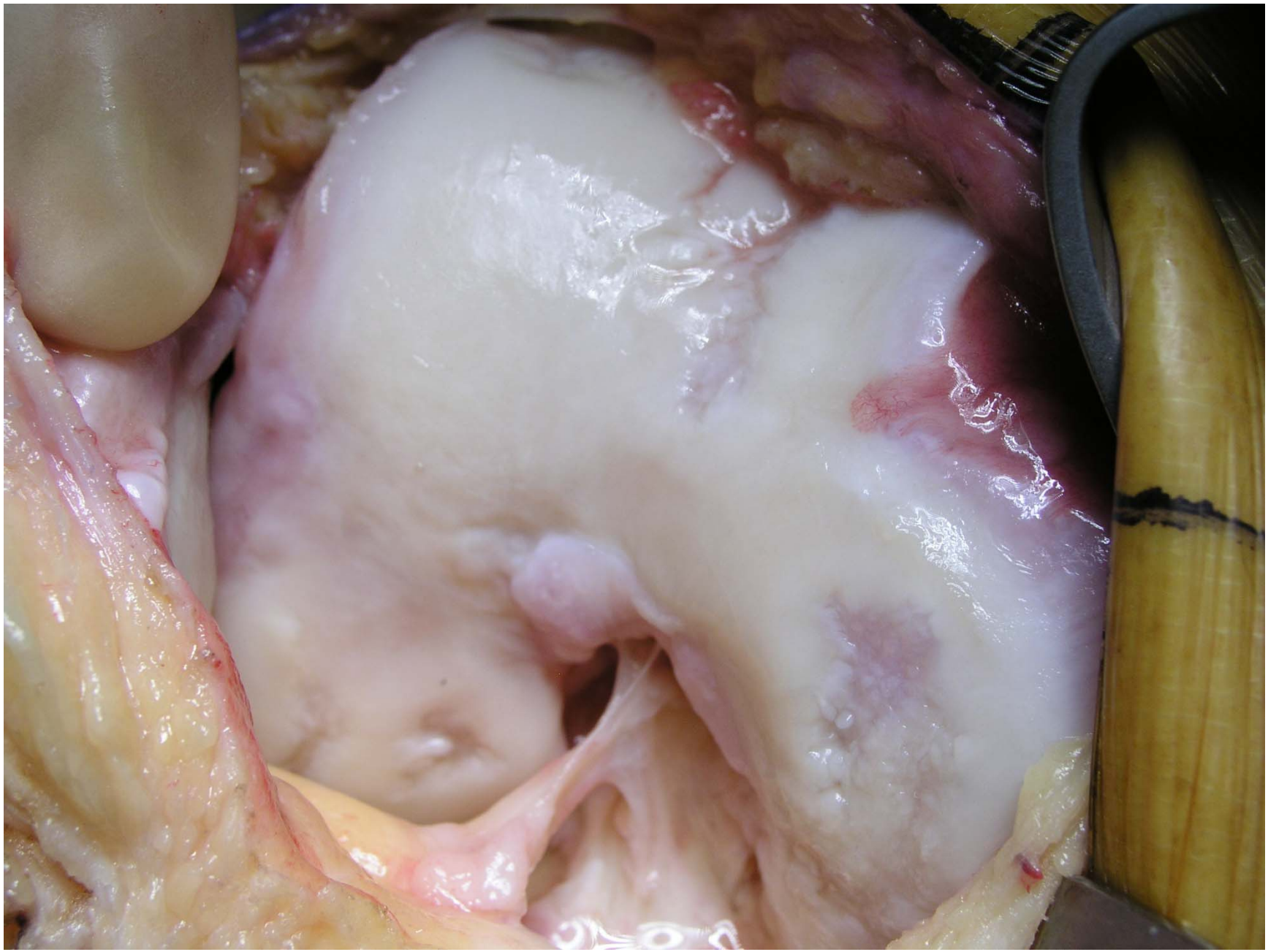


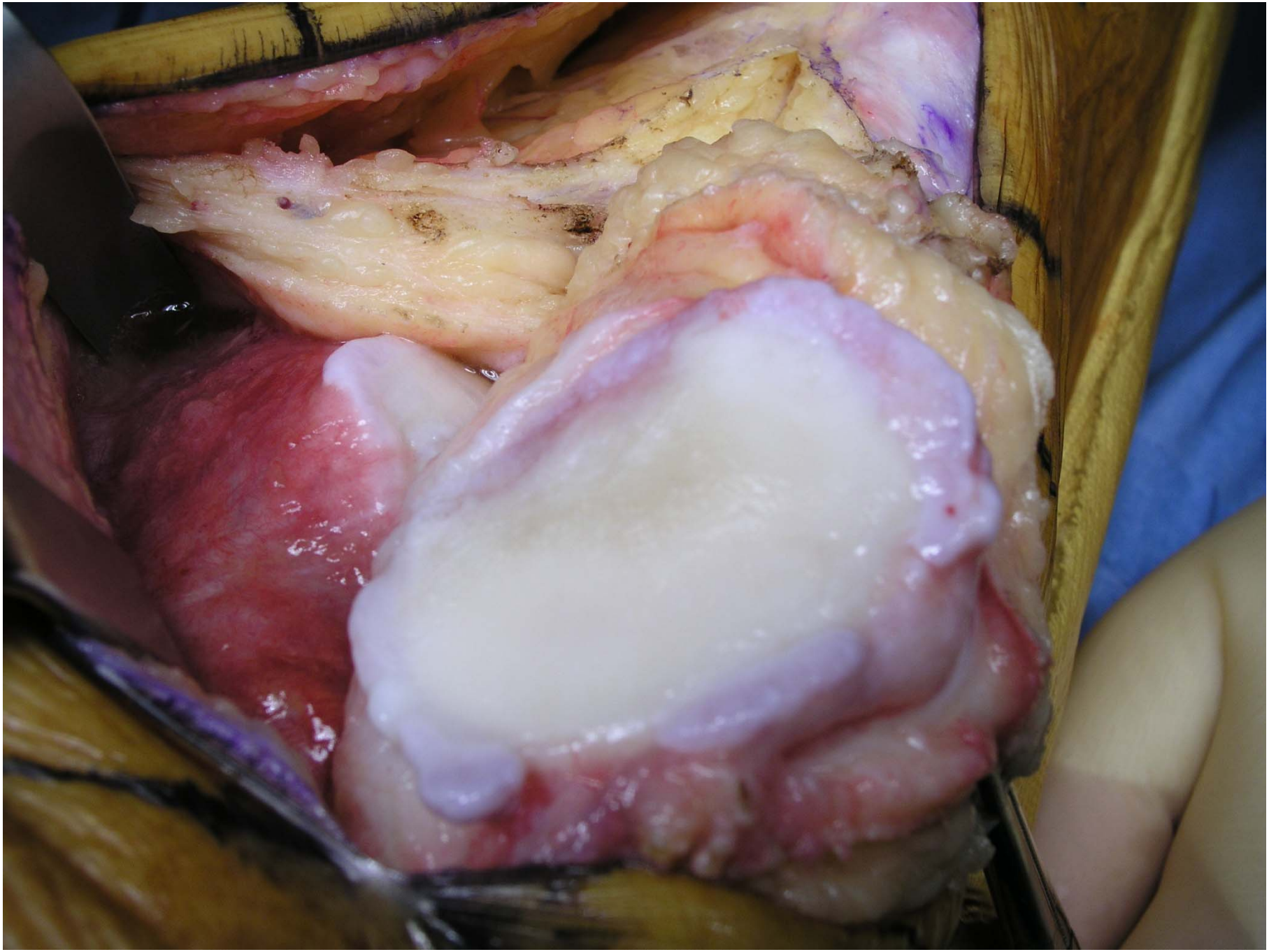


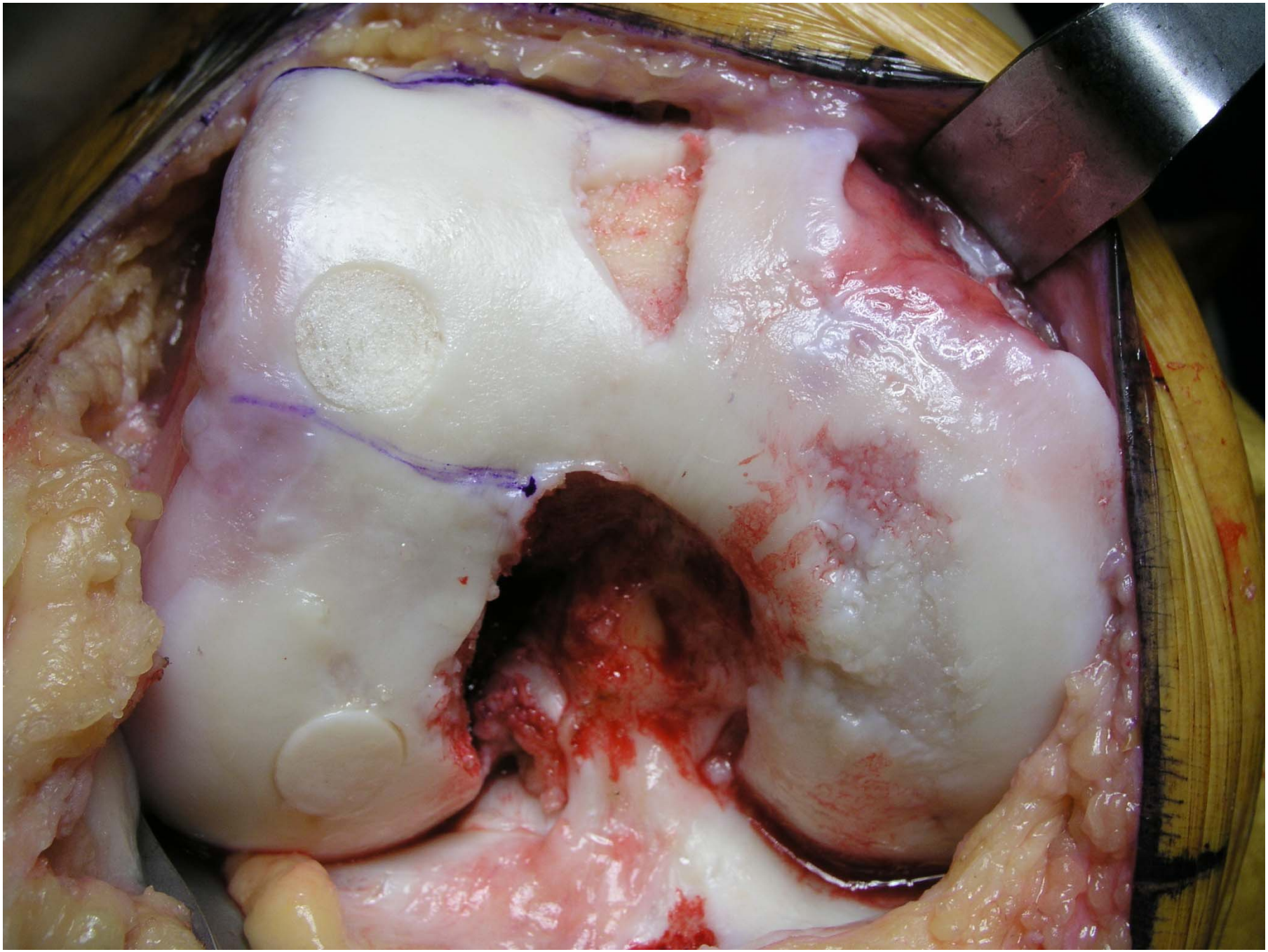


Case 3

- 46 male





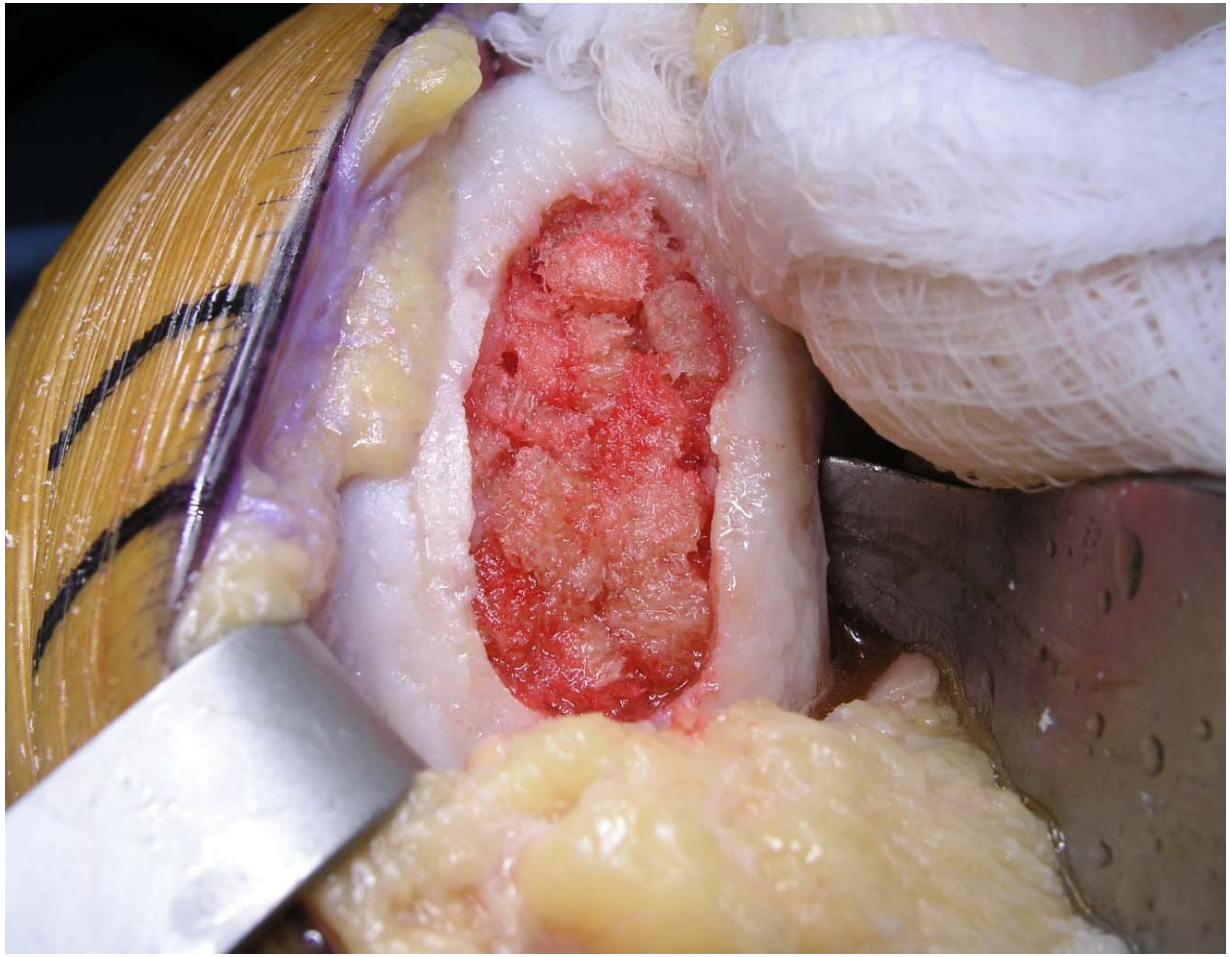


Case 4

39 female

[L]


Se:1
Im:2
D.JAMES, A
Study Date:11/30/2004
Study Time:7:05:52 PM
MRN:
C2048
W4096



Results of salvage ACI in early OA

T Minas 2003 *Orthopedics*

- 71 salvage cases
- Mean age 40
- All had early OA
  - <50% joint space narrowing
  - Bipolar kissing lesions
  - Peripheral osteophytes
- Too young for TKA

Results of salvage ACI in early OA

T Minas 2003 *Orthopedics*

- Average follow-up 4 years (2-7)
- 12 (17%) further surgery
- 2 (3%) required TKA
- Cincinnati Knee Score (means)
  - Pre-op 3.1
  - Post-op 5.2 ($p<0.001$)

What do we think?

ACI for OA

- ACI unproven in treating simple cartilage lesions
- No controlled data on ACI use in treating OA
- No present RCTs
- Expensive
- EXPERIMENTAL

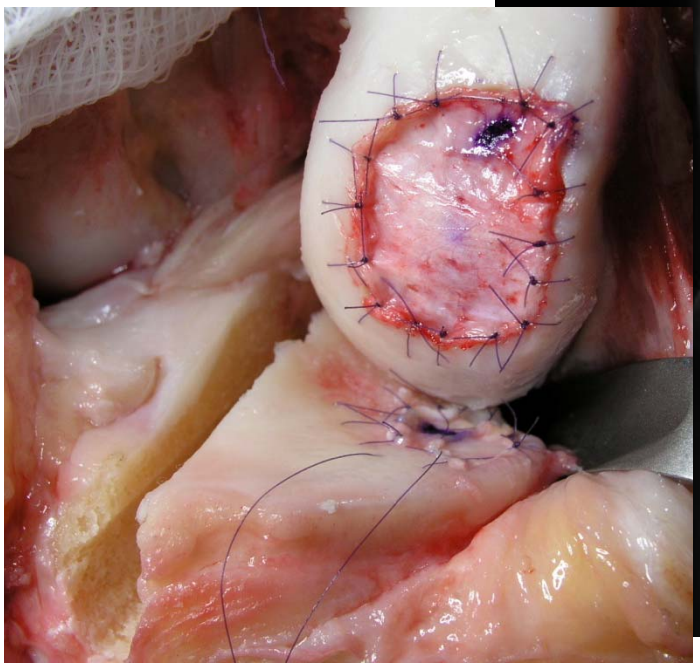
MADNESS

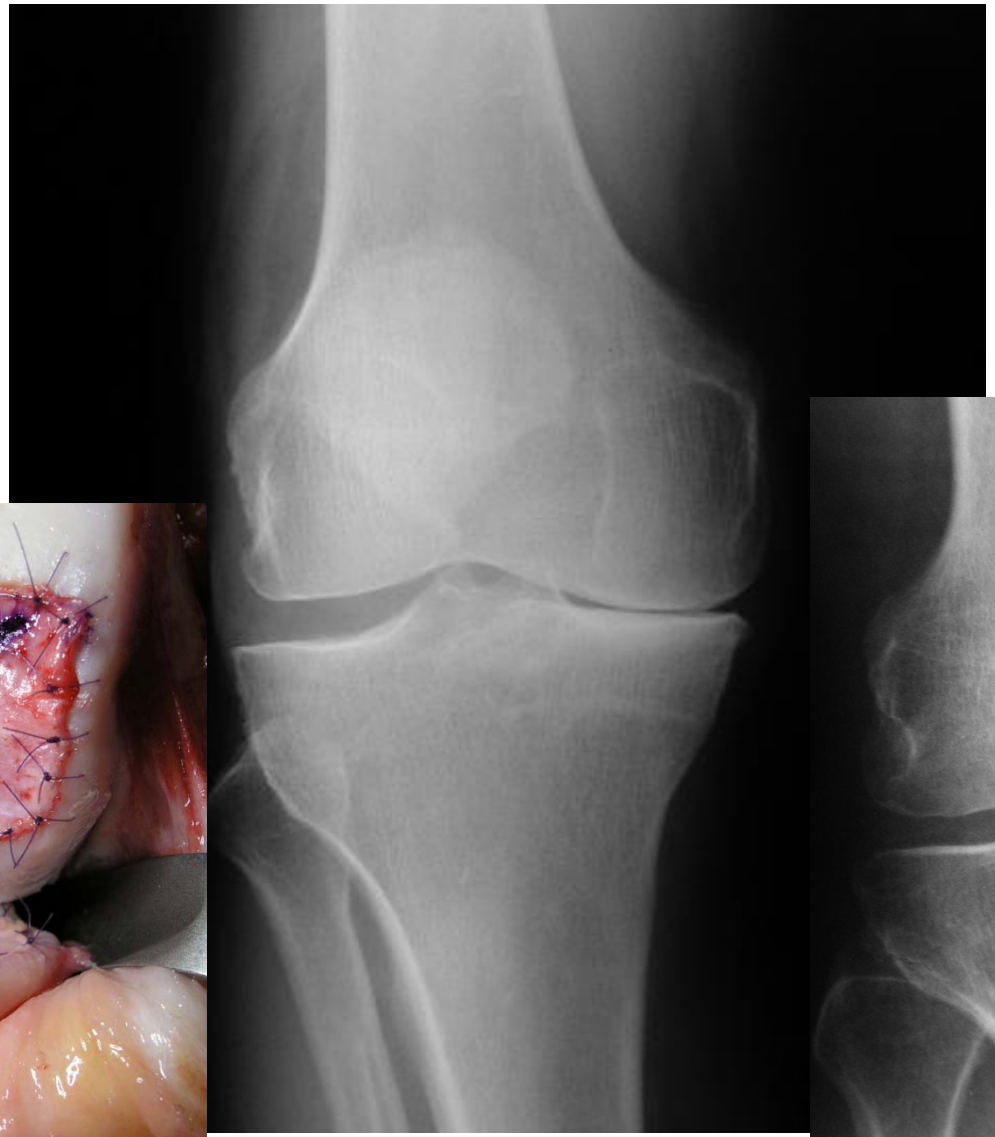
ACI for OA

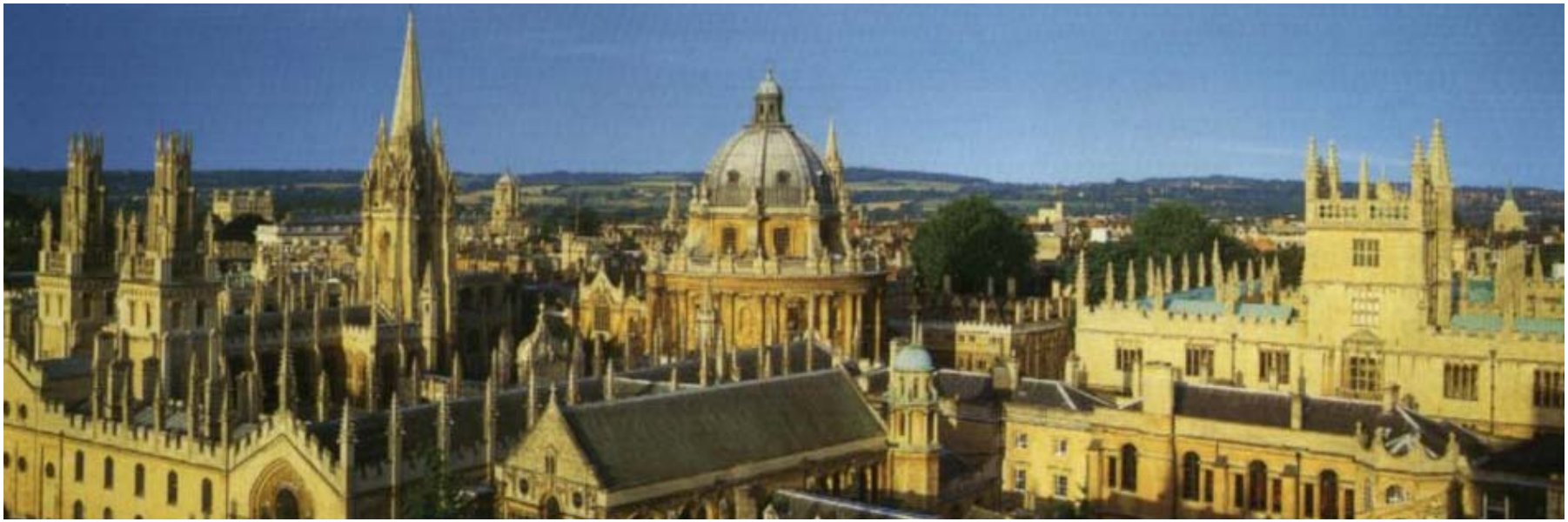
- Pioneering
- Biological treatment will develop
- Improved biological materials
- Improved manipulation of cell function
  - Growth factors, Gene treatment
- In-situ treatment

THIS IS THE FUTURE…

Will cartilage transplantation replace UKA?







Thank you


P
A

Nuffield NHS
Orthopaedic Centre
NHS Trust

Cartilage Transplantation in the Knee

Treating Early Osteoarthritis

Andrew Price
DPhil FRCS(Orth)

Consultant Orthopaedic Surgeon
Reader in Musculoskeletal Science
Nuffield Orthopaedic Centre
Nuffield Department of Orthopaedic Surgery
Oxford University

BRC

NHS
National Institute for
Health Research

Clinical Scientist

Clinical treatment

Basic science research

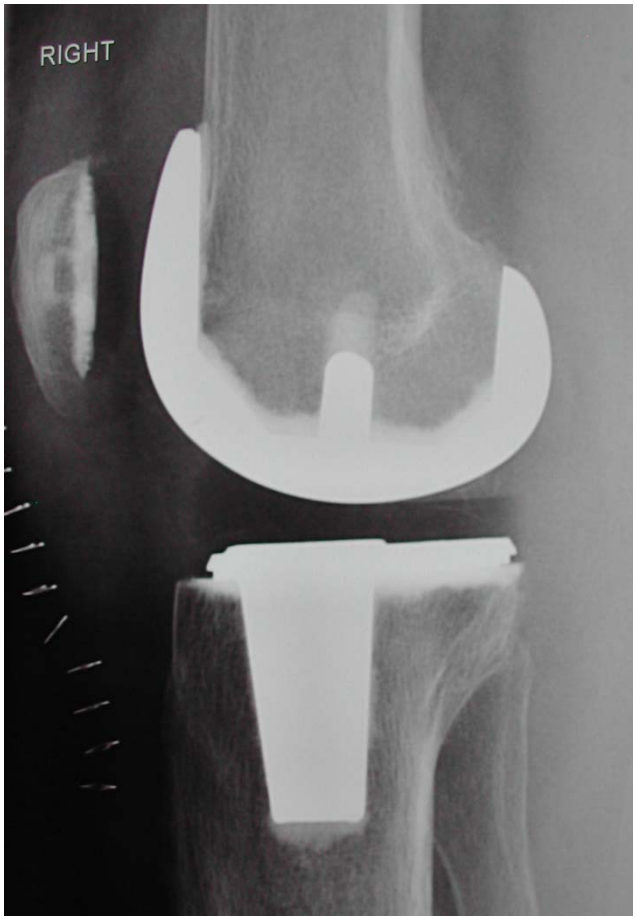
Cartilage disease in the knee

Co-investigators

J Rees, D Beard, B Robinson, N Arden, C Cooper, K Javaid R Gill, A Zavatsky, P Oppold, A Short, C Kellett, B Marks, H Pandit, C Dodd, JJ O'Connor, J Goodfellow, P McLardy-Smith, R Gundle, R Rout, S McDonald, C Dodd, D Murray, A Carr, M Thompson, N Athanasou, P Hulley, D Simpson, M Gibbons, D Whitwell, G Moxley, J Loughlin, A Taylor, Z Xia, J Triffitt, S Snelling

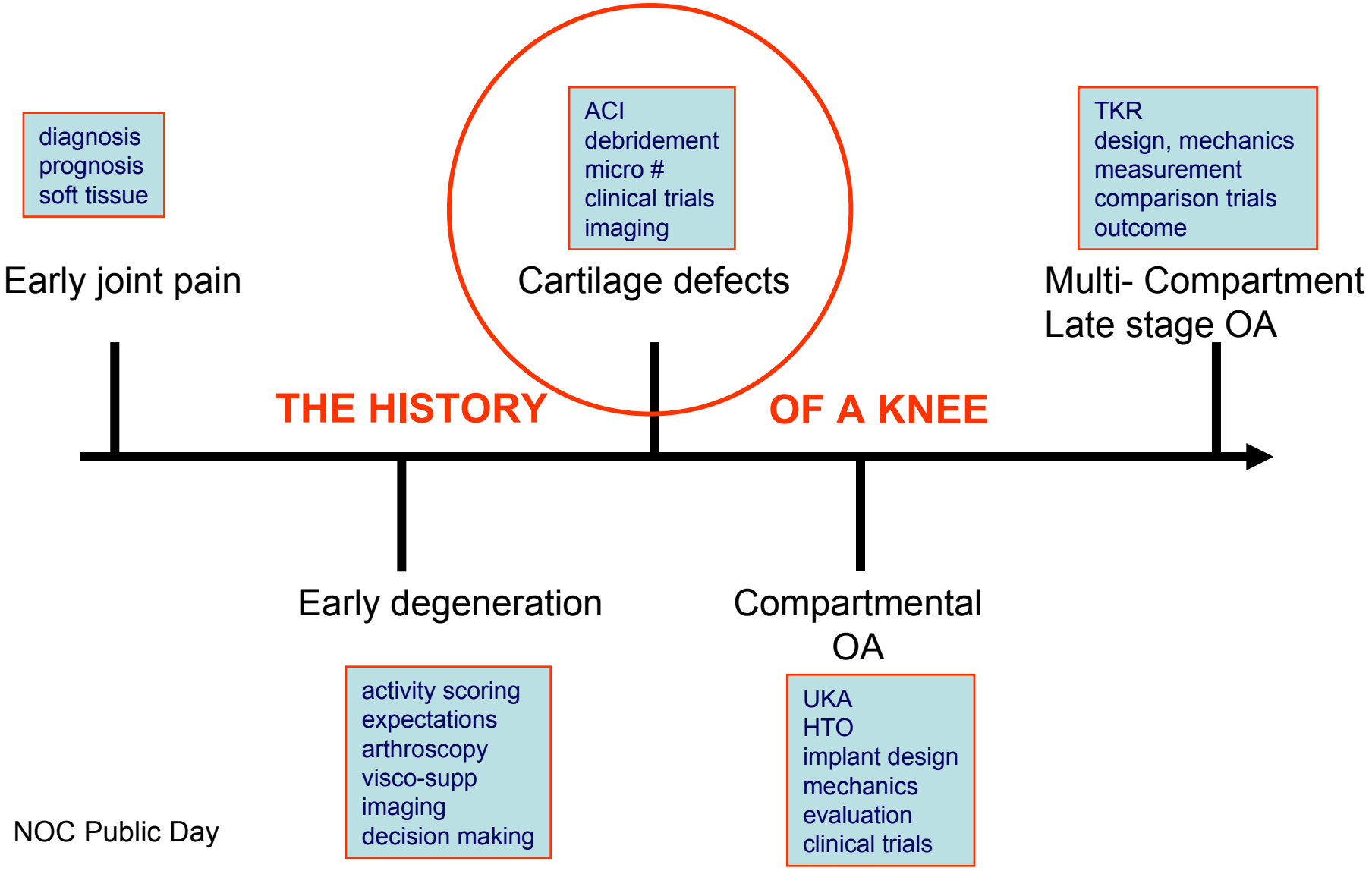
Osteoarthritis

Total knee replacement



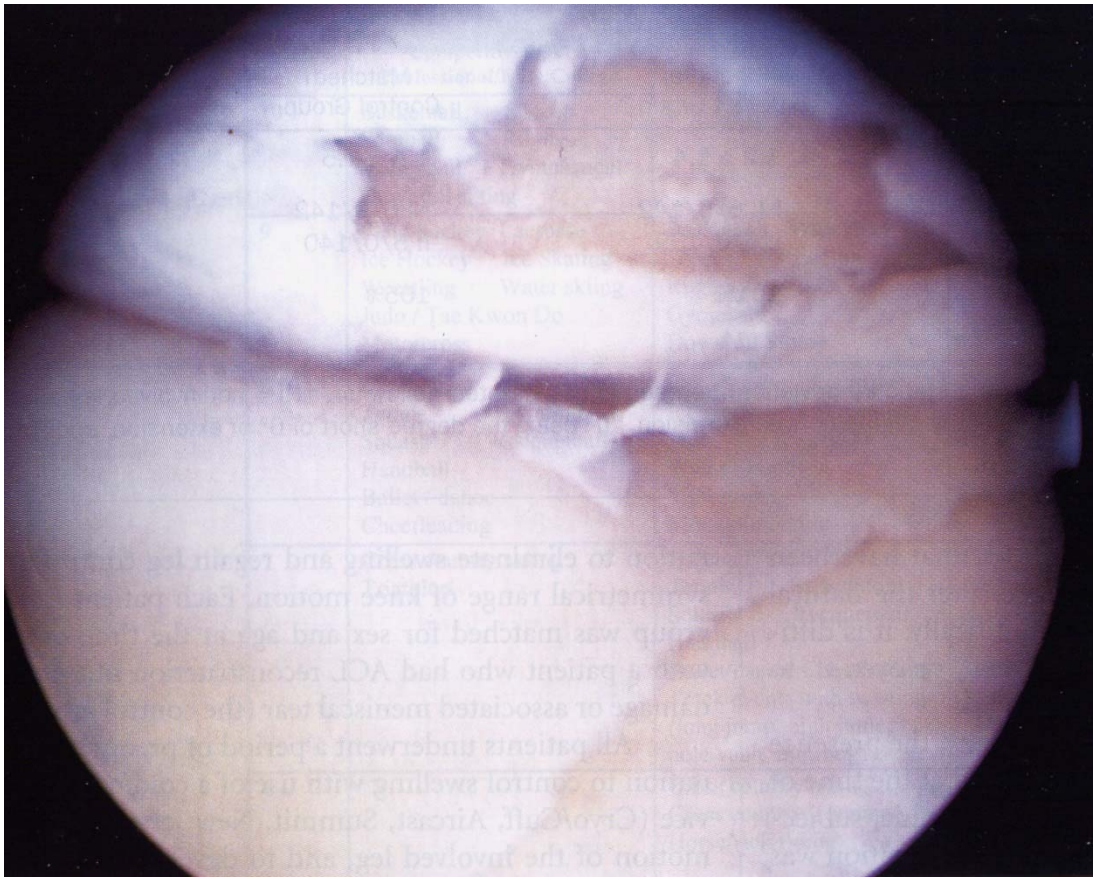
Price, Beard, Gill,
Murray, Dodd, Pandit
(Fellows & Collaborators)

Oxford Knee Research Programme



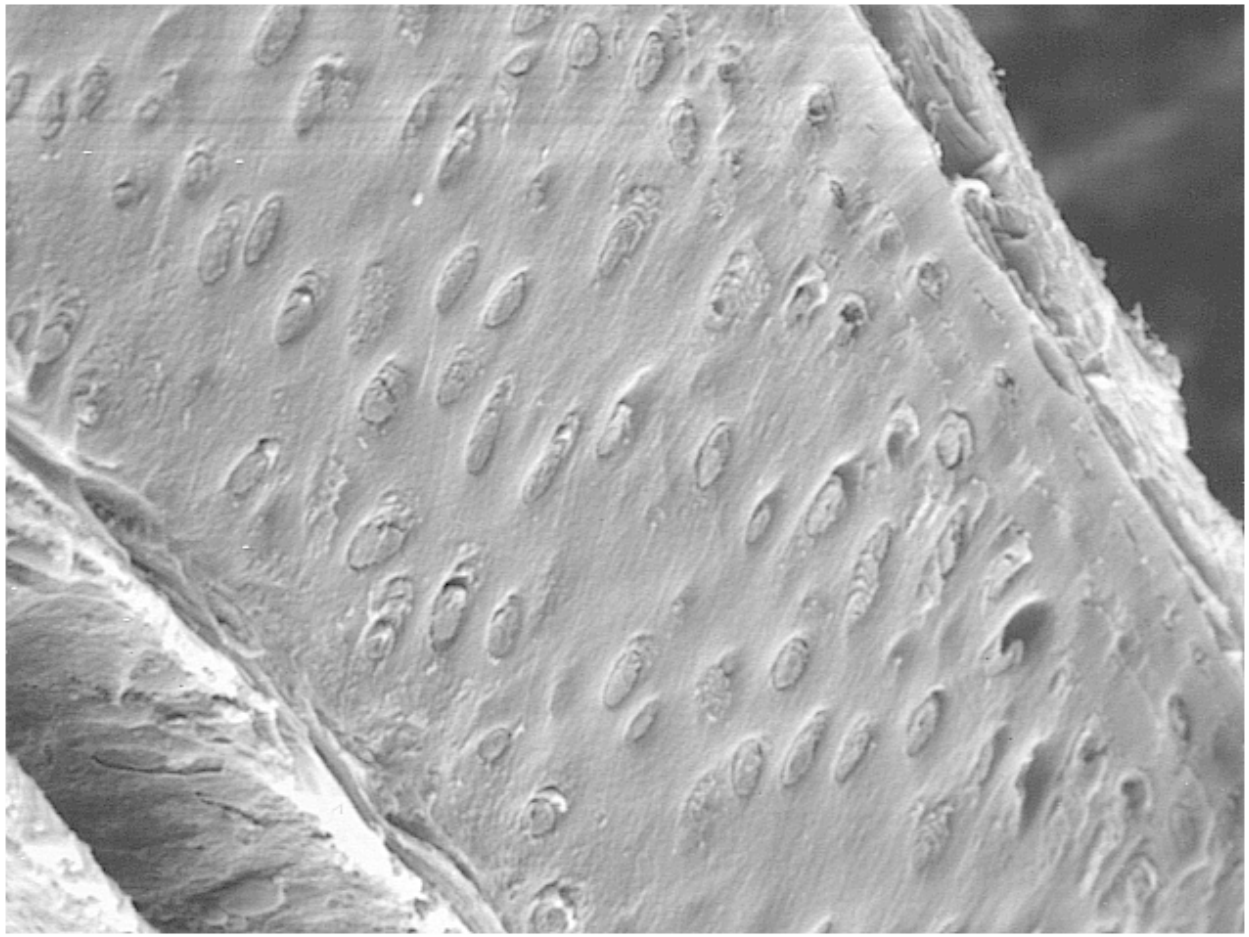
Isolated cartilage defect

Pain and disability

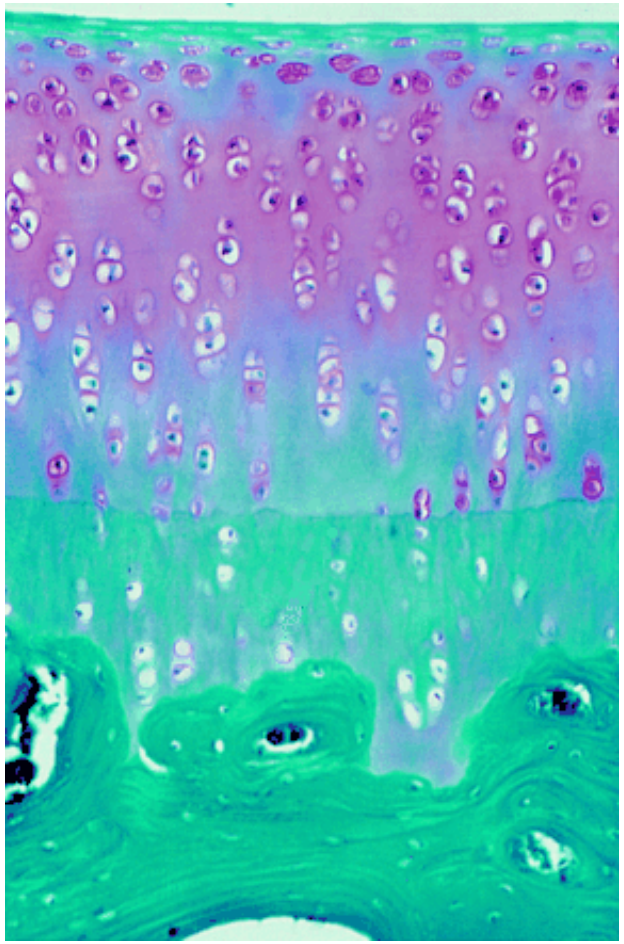


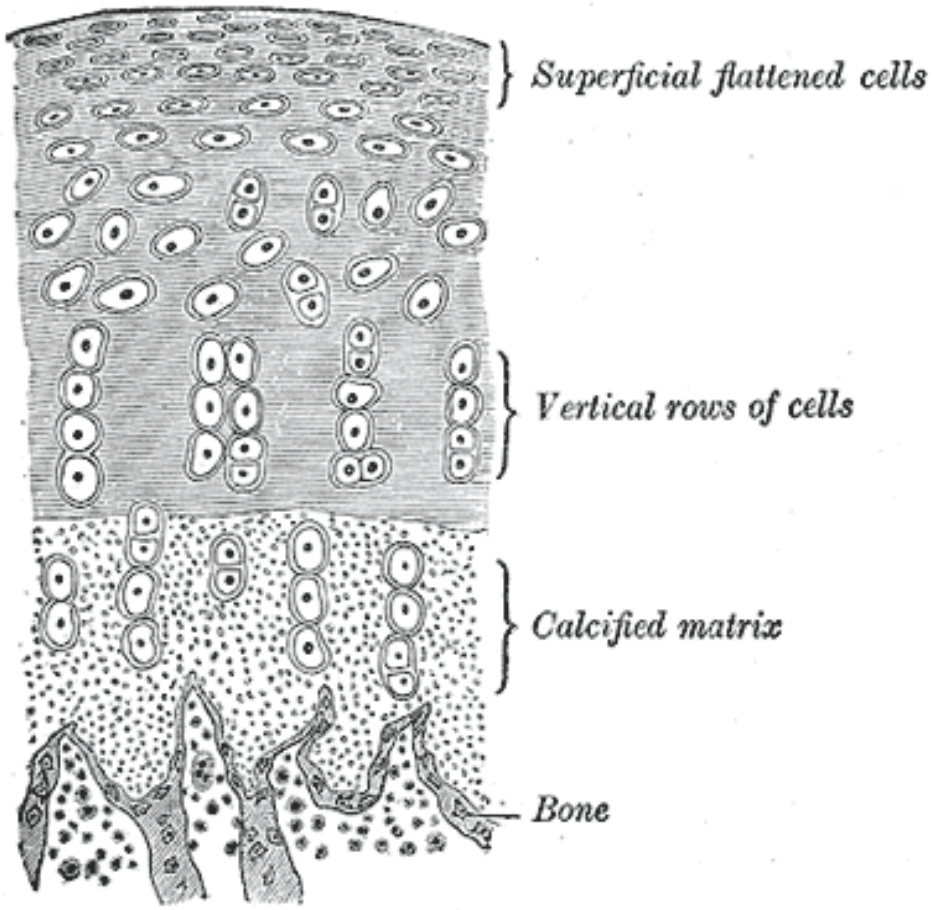
Cartilage structure

Cartilage



Cartilage




Superficial flattened cells
Vertical rows of cells
Calcified matrix
Bone

Cartilage repair techniques

Drilling

Cartilage/bone grafts

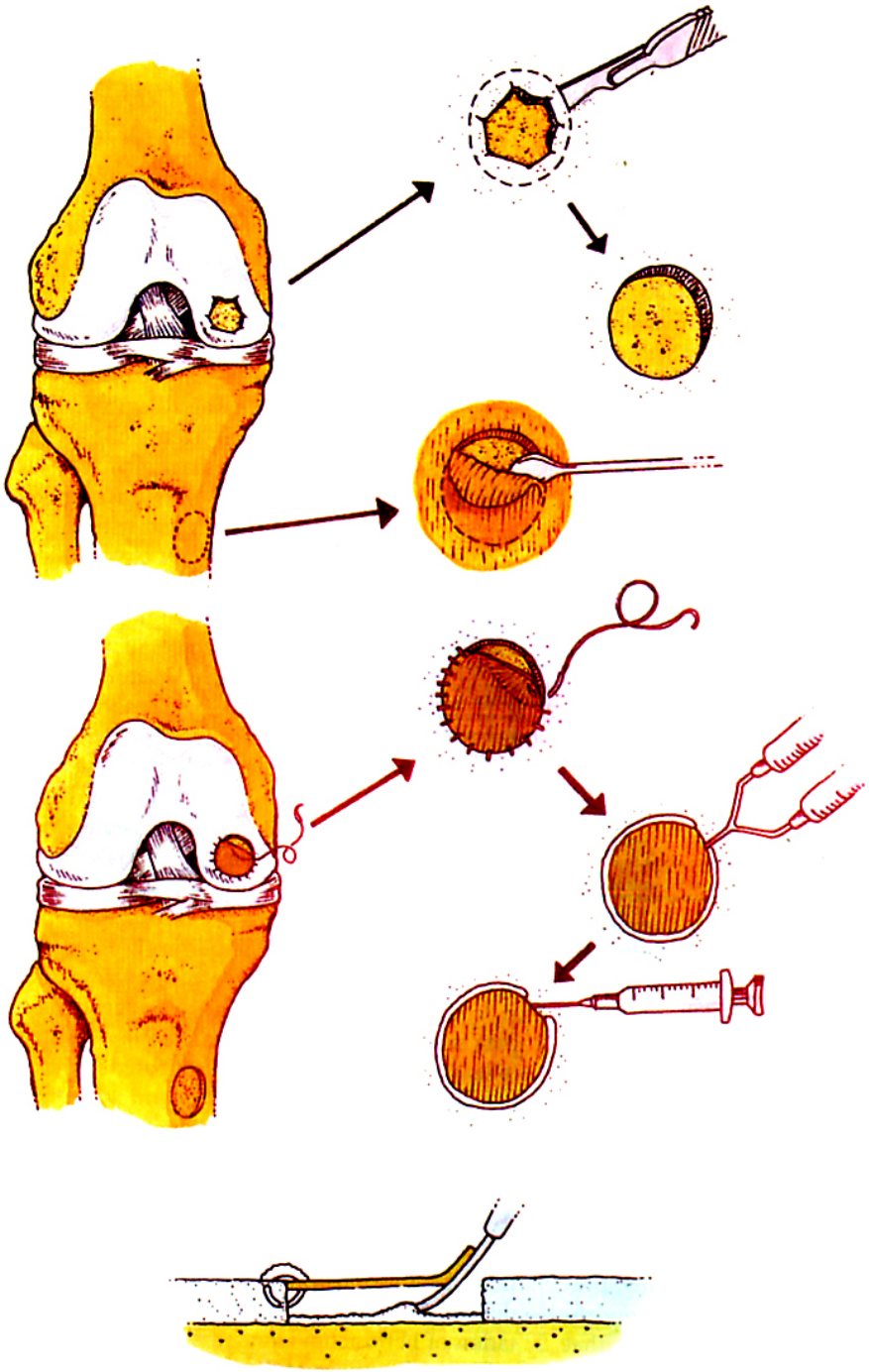
Implanting cartilage cells

Cartilage repair techniques

Drilling

Cartilage/bone grafts

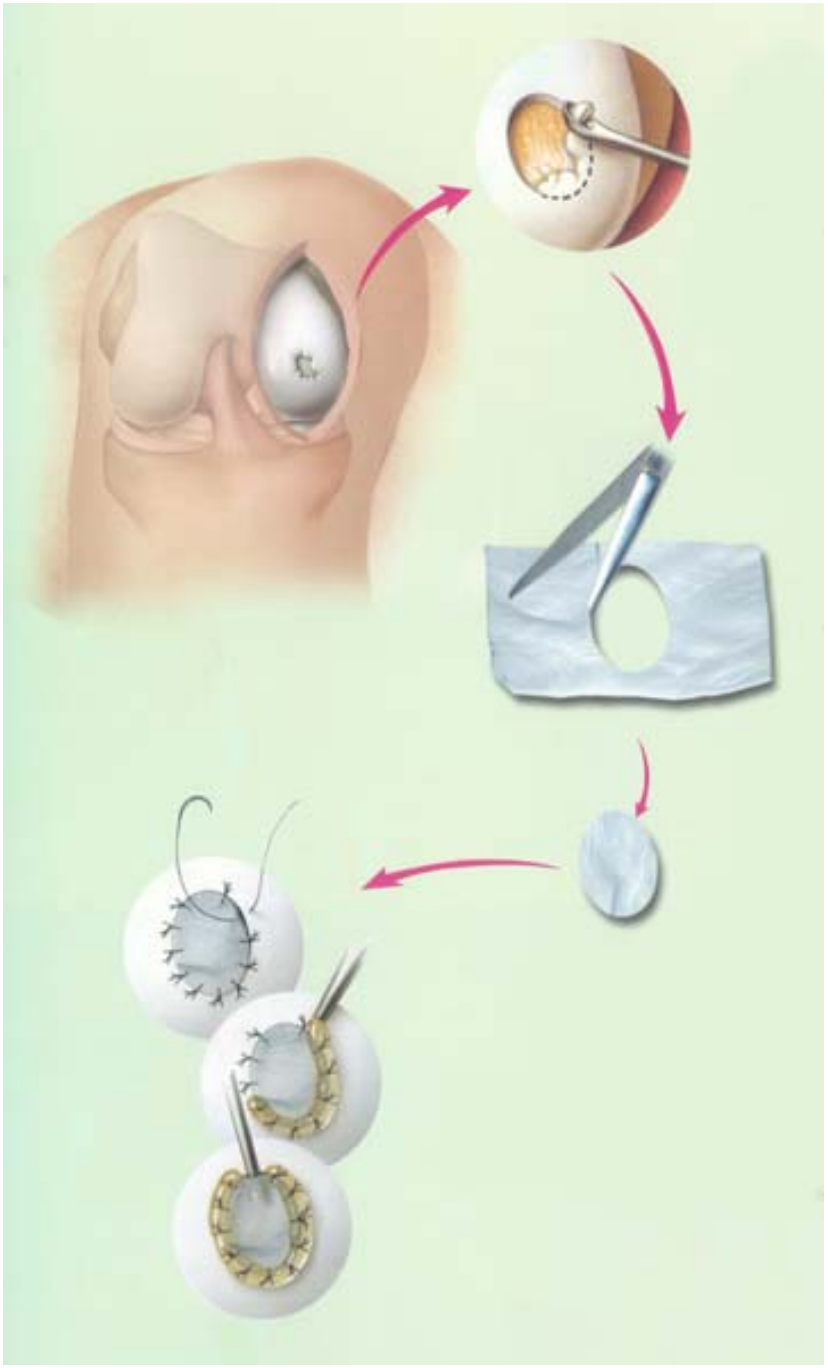
Implanting cartilage cells



Autologous
Chondrocyte
Implantation

“ACI”

Lars Peterson
technique - 1987



Autologous
Chondrocyte
Implantation

- new technique

National Institute of Clinical Excellence
(NICE)

Guidelines

All cases must be performed
as part of a clinical trial

Stanmore ACI Trial

Randomised controlled trial
Compares two ACI methods

Questions addressed:

Is the technique clinically effective?
Which is the best method?

Introducing ACI to the NOC

Process

NOC Rare Procedures Committee
Oxford Ethics Committee
NOC Research & Development Committee
NOC Orthopaedic Directorate Board

9 Months

NICE

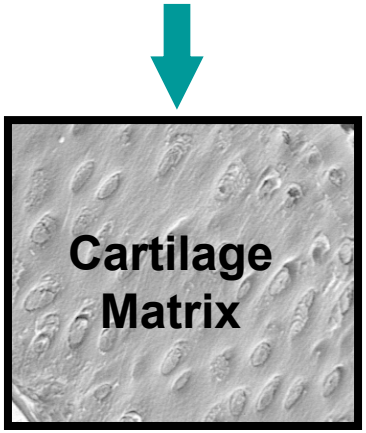
ACI review

Further basic science research required

Greater understanding of growth factors and agents that influence cartilage cell function

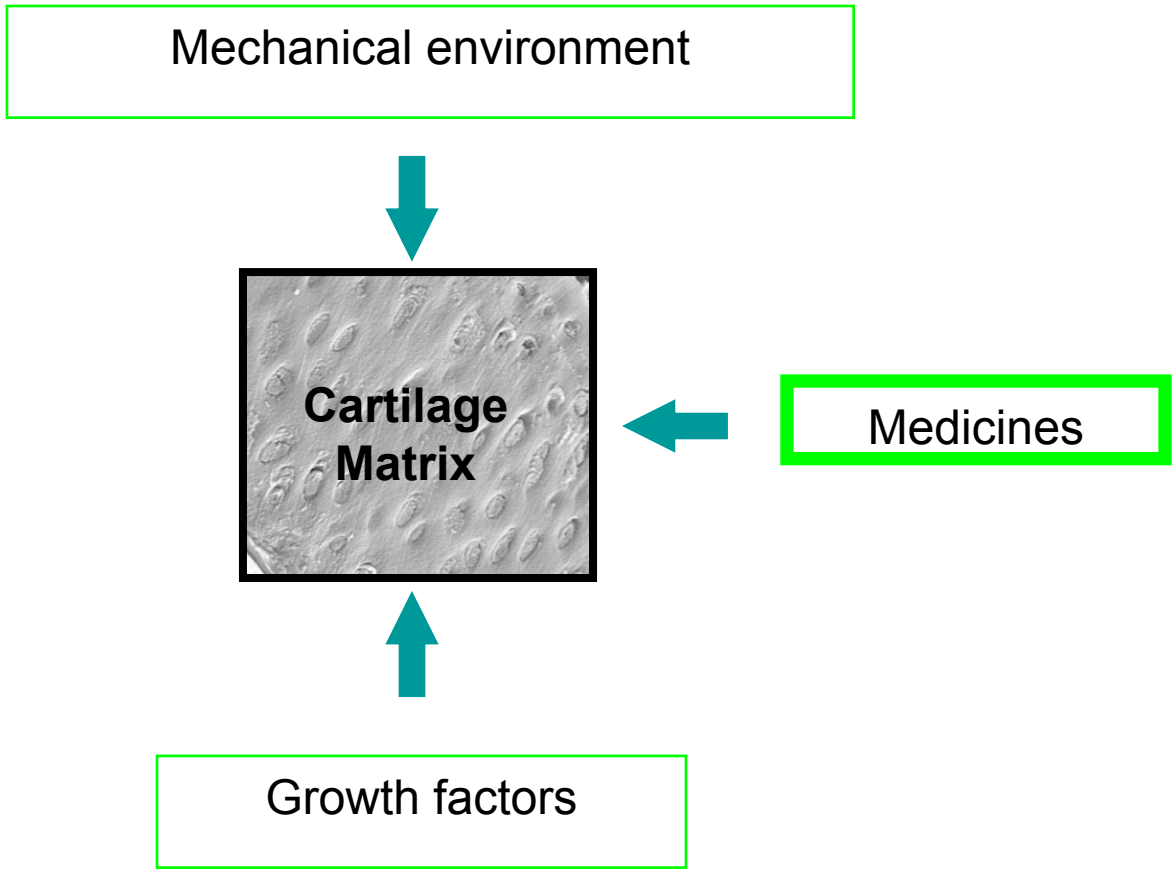
Cartilage

Mechanical environment



Growth factors

Cartilage

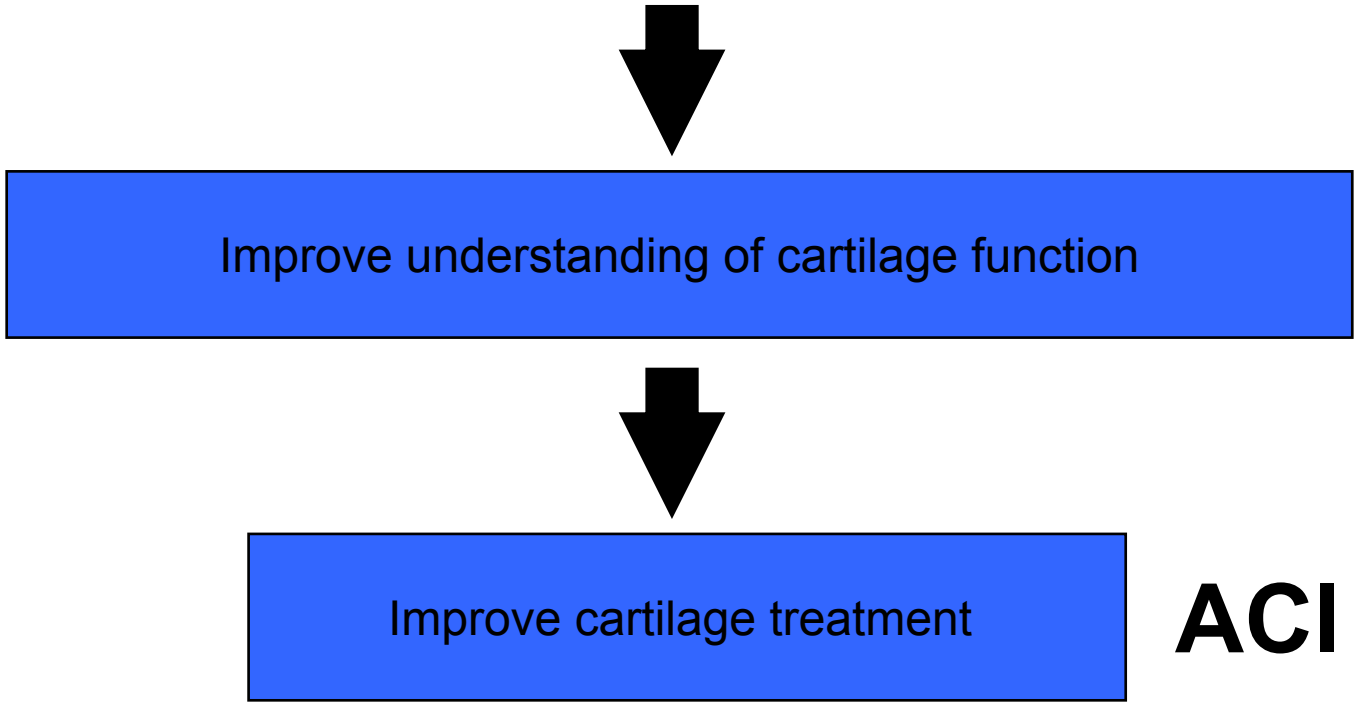

Mechanical environment
Cartilage Matrix
Medicines
Growth factors

Basic Science

(Dr Philippa Hulley, Dr Richie Gill)

Action of load and growth factors

Action of drugs/medicines



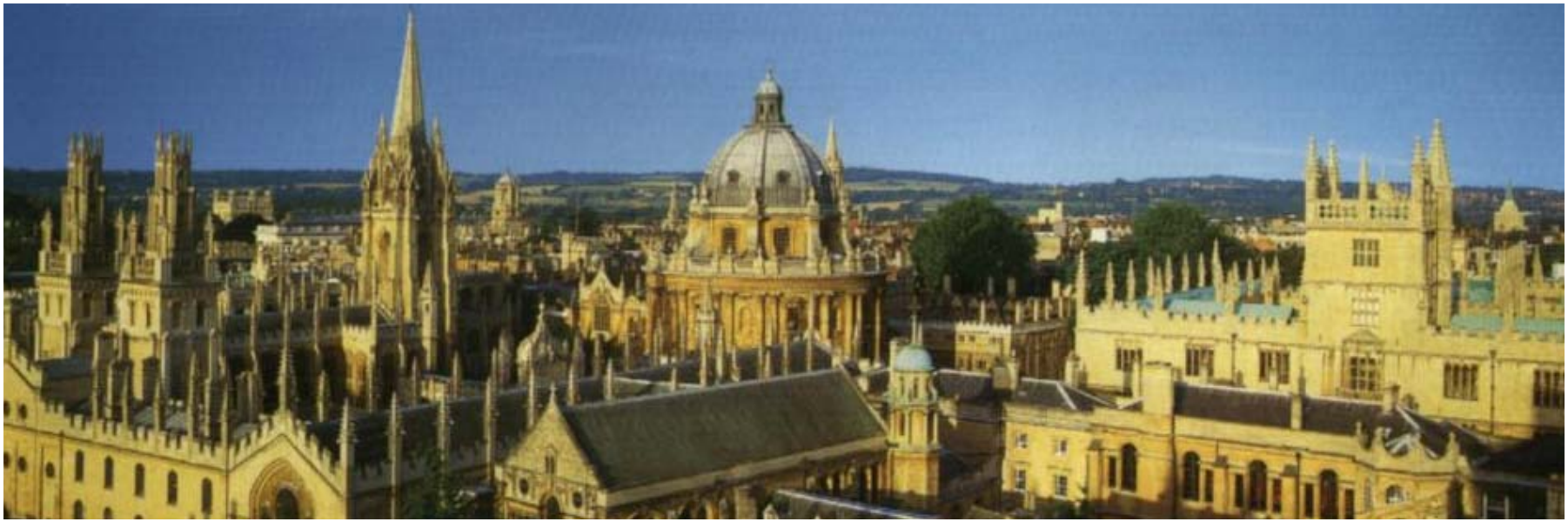
Laboratory experiments

Human cells required for studies

Cartilage is removed at
joint replacement

Patients asked to donate this
material to allow us access to
human cartilage cells

Ethics committee approval



Thank you