The Management of articular cartilage defects

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Summary

• Cartilage heals poorly, to fibrocartilage

• Natural history unknown

• Many treatment options, poor follow-up

• Controlled prospective clinical trials needed
Articular Cartilage

- Chondrocytes and Matrix
- Type II Collagen, proteoglycan, 70% Water
- 3-D Structure - 4 Layers
- Mechanically strong, non-vascular

- Hunter 1743 “Once destroyed, not repaired”
Response to Injury

FULL THICKNESS
- Blood, Fibrin clot
- Chondroid Metaplasia
- Fibrocartilage, with 30% type I Collagen
- Degenerates over 6/12, fibrillation

PARTIAL INJURY
- Adjacent necrosis
- brief period of mitosis
- ceases by 2/52
- no longterm healing
- ? PROGRESSION
Response to Injury

- Size of Defect (<3mm - gradual healing)
- Depth of Defect
- Subject age
- Role of CPM
- Underlying pathology
Response to Injury

- Natural history unknown, ?asymptomatic lesions

- Messner & Maletius 1996 (Acta Orthop)
  - 28 young athletes, 14 year F/UP
  - 10 without Rx
  - No clinical difference between index and contralateral knee, no radiographic changes.
Therapeutic Options

• Shaving, debridement
• Abrasion / micro# / drilling
• Osteotomy
• Transplantation of auto/allograft; osteochondral perichondrium periosteum chondrocytes
Therapeutic options continued

- Synthetic materials
  - carbon pads / rods
  - gels, transport medium
  - polylactic and polyglycolic acid mesh
- +/- adhesives (e.g. fibrin glue), and C.P.M.
- Pharmacology
Shaving and Debridement

- Removes unstable flaps
- Reduces mechanical blocks / locking
- No evidence of stimulation to repair
  Kim JBJS 1991
- Documented boundary fibrillation and necrosis
Abrasion / Micro# / Drilling

- Pridie JBJS 1959
- Introduces vascularity, clot, cytokines and growth factors
- Results are unpredictable, tend to deteriorate
  Buckwalter JBJS 1997
- Many advocates, e.g.; Blevins Orhtopaedics 1998
  used in athletes, 3 year F/UP, + CPM
Tissue Transplantation

- ALLOGRAFT
  - Cadaveric
  - orthotopic - contour
  - Osteochondral, risk of infection + rejection?
  - Storage = deterioration

- AUTOGRAFT
  - Donor morbidity
  - limited supply
  - fixed age of donor!
  - Poor contour match
Osteochondral allograft

- Beaver et al., JBJS 74B 1992
- 100 patients, large osteochondral defects
- fresh cadaver graft, with corrective osteotomies.
- Results - 75% good @ 5 yrs, 63% @ 14 yrs
- advise other Rx in ostoeochondritis, OA.
- Best result found in young recipients/trauma
Osteochondral autografts

- Using multiple plugs, ie Mosaicplasty
- Gaps fill with fibrocartilage
- Outerbridge JBJS 77A 1995
  10 ‘large’ femoral defects, 6 yr F/UP
  Cincinnati knee score 43 ◆ 93.

- Hangody Orthopaedics 1998
  57 patients (68% concomitant Rx, mixed aetiologies), F/UP @ 3 yrs.
  HSS score 90 (?pre-op score, ?histol)
Perichondrial grafts

• Reduce donor site morbidity by using other source of chondrogenic cells
• Early clinical trials
  Homminga JBJS 1990
costal perichondrium glued with fibrin
25 pts., 30 lesions, 2nd look @ 1 yr
90% filled with ‘cartilage’, NO CELLS
Periosteal grafts

- *In Vitro* periosteum at low pO2 produces articular cartilage.
- Salter & co-workers have implanted rabbit lesions, then CPM, then analyse @ 1 year
- Cell clusters in 33%, BUT abnormal collagen and ghost cells/empty lacunae

O’Driscoll JBJS 1988
Moran JBJS 1992

- Few clinical results
Mesenchymal stem cells

- Site-specific differentiation, thus could recreate 4-layer structure?
- Holtzer 1960 - able to ‘de-differentiate’ adult cells - reversible
- Wakitani JBJS 1994 - Rabbit model hyaline cartilage regrowth mechanically strong = host tissue BUT incomplete integration
Synthetics “designer cartilage”

- Man-made scaffold seeded with cultured chondrocytes
- could replace whole condyles?
- malleable, insert arthroscopically?

- *In Vitro* use of fibrinogen, collagen, carbon fibre, PGA, PLA (Chu, 1995)
Synthetic, continued...

- Clinical results

- Muckle & Minns JBJS 1990
  carbon pads, 47 patients; fill with strong fibrous tissue (=fibrocartilage)
  independent review (Bentley 1992) 79%
  ‘better’ (analogue pain scores)

- Brittberg Clin Orthop 1994
  carbon, 36 pts., 4 yr. F/UP for early OA
  results good/excellent in 83%
Pharmacology

• Numerous *in vitro* studies

• Growth factors, BMP-2, cytokines, protease inhibitors, TGF-β.

• No clinical results
Chondrocyte transfer

- Smith 1965 Nature; Isolation of articular chondrocytes
- Bentley 1971 Nature
  Cell transfer (rabbit model); cells survived, matured, produced matrix
- Aston & Bentley 1986 JBJS 68B
  rabbit harvest, culture and transplant
  64% incorporation @ 1 year
Chondrocyte transfer, cont...

• Brittberg 1996 Clin Orthop 326
  Chondrocyte cover under periosteal flap
  4 groups; +/- chondrocytes
  +/- carbon fibre scaffold
  Best results with cells, no carbon fibre
  (histological assessment only)
  Boundary fissures observed
Figure 1. Diagram of Chondrocyte Transplantation in the Right Femoral Condyle. The distal part of the femur and proximal part of the tibia are shown.
Chondrocyte transfer, cont...

- Brittberg 1994 NEJM 331
- Same method, in 23 patients, ave. age 27 defects 1.6-6.5 cm², + pain/locking
  Post-op all symptoms resolved
- 2nd look arthroscopy @3 yrs.
  Graft integration, no ‘waves’, firm
  Biopsy - hyaline cartilage in 11/15
Figure 2. Results of Autologous Chondrocyte Transplantation in a 22-Year-Old Woman (Patient 9). Panel A shows the cartilage defect in the medial femoral condyle before cell transplantation. Panel B shows the defect (1.1 by 4.0 cm) 46 months after transplantation. The borders of the transplant are indicated by the arrows. Knee surgery was performed at 46 months because of patellar trauma that was unrelated to the transplantation.
Chondrocyte transfer, cont....

- Flaws to study;
- Not controlled, randomised, short F/UP
- No independent knee scoring, eg HSS
- Mainly small lesions (?non-progressive)
- Cartilage not quantified (durability), no collagen ratios
- Outcome - ?any better than debridement
The future

• Use of newer transport media;
  Frenkel JBJS 1997 - Bilayer collagen
  Rahfoth Osteoarth 1998 - Agarose gel
to stop de-differentiation

• Improved initial stability
  Brittberg Biomaterials 1997 - Fibrin
  adhesive   repair, blocks migration
Conclusions

• Articular cartilage defects heal poorly
• “Completing” the defect produces fibrocartilage, which is suboptimal
• Cartilage transplantation remains unproven and unpredictable
• Synthetic matrix / pharmacology may help
• Long term randomised trials are needed
Thankyou