Augmentation Techniques for Meniscus Repair

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Abstract

Menisci display exquisitely complex structure and play an essential weight-bearing role in the knee joint. A torn meniscus is one of the most common knee injuries which can result in pain and mechanical abnormalities. Tear location is one aspect which determines the endogenous healing response; tears that occur in the peripheral densely vascularized zone of the meniscus have the potential to heal while the healing capacity is more limited in the less vascularized inner zones. Meniscectomy was once widely performed, but led to poor radiographic and patient-reported mid- and long-term outcomes. After the advent of arthroscopy, orthopaedic opinion in the 1980s has been swaying toward salvaging or repairing the torn meniscus tissue to prevent osteoarthritis rather than performing meniscectomy. Meniscus repair in young active individuals has been shown to be effective, reproducible, and reliable if indications are met; however, only a small proportion of all tears are considered repairable with available technologies. Biological augmentation techniques and meniscus tissue engineering strategies are being devised to enhance the likelihood and rate of healing in meniscus repair. Preclinical and clinical studies have shown that introduction of cellular elements of the blood, bone marrow, and related growth factors have the potential to enhance meniscus repair. This article reviews the current state of clinical management of meniscus tears (primary repair) as well as augmentation techniques to improve healing by meniscus wrapping with extracellular matrix materials, trephination, synovial rasping and abrasion, fibrin/blood clot placement, and platelet-rich plasma injections. In addition, the rationale for using polymer/autologous blood component implants to improve meniscus repair will be discussed.

Keywords
► meniscus repair
► augmentation techniques
► platelet-rich plasma
► chitosan

Menisci are semilunar-shaped fibrocartilaginous structures[1,2] that play central load bearing and load distribution roles in the knee joint.[3] Population-based data suggest that meniscal damage is present in at least one-third of the knees of middle-aged or elderly individuals[4] and meniscus-deficient knees are more likely to develop radiographic evidence of osteoarthritis (OA)[5] and increased degeneration over time.[6] Although there has been a recent increase in the number of meniscus repairs performed yearly in the United States,[7] only a small portion of all meniscal tears are considered repairable so that current surgical treatment of symptomatic meniscal tears often involves partial removal of torn meniscus, which increases the risk of developing OA.[8–10] Tear properties such as tear pattern, length, depth, size, stability, location (medial vs. lateral and where geographically in each), chronic or acute, patient profile (age, health, symptoms), and joint stability are

all important factors affecting the rate of healing and should be considered before patients undergo meniscus repair.

One of the major impediments in repairing a damaged meniscus is that only the outer rim of the tissue is vascularized.[11–13] Since wound healing in adult tissues is triggered by the products released with blood clotting, the capacity for natural repair is optimal in the periphery of the meniscus and diminished in the inner margins.[14] Tear location thus becomes critical, and tears occurring in the peripheral vascularized portion of the meniscus are the most amenable to healing and thus, repair. Healing is more difficult in the case of other tear patterns such as radial, horizontal, fragmented, or white–white (W-W) displaced bucket handle and in the case of complex, chronic, or degenerative tears.[15,16] When meniscal tears occur in the peripheral vascularized area of the meniscus, repair by suturing leads to satisfactory clinical improvement in 70 to 90% of patients. Nonetheless, the clinical failure rate can be as high as 20 to 24% depending on, among other factors, the status of the anterior cruciate ligament (ACL),[17] while incomplete healing corresponding to structural failure is yet higher than the clinical failure rate.[18] Although previously considered to be irrepairable, the current trend is to suture tears that occur in the inner nonvascularized margins, with reports of surprising clinical success in up to 68% of patients,[19] while here again structural failure can be much higher. There remains a need to develop reproducible and efficient meniscus repair augmentation techniques. The purpose of the current review is to describe the current clinical management of meniscus tears and different repair augmentation techniques that are available including meniscus wrapping with extracellular matrix (ECM) materials, trephination, synovial rasping, and abrasion, as well as application of exogenous fibrin/blood clots and platelet-rich plasma (PRP). Finally, the rationale for using chitosan–PRP implants to improve meniscus repair will be discussed.

Current Clinical Management of Meniscus Tears

Meniscus tears are among the most common type of knee injuries,[20,21] and treatment of meniscal tears accounts for half of the arthroscopic procedures performed in the United States.[22] Overall, meniscus tears fall into two overlapping categories: either traumatic or degenerative.[15] Age, gender, work-related kneeling, squatting, or climbing stairs are among the risk factors for developing degenerative tears, while acute meniscal tears tend to be sports-related[23] understanding that an acute tear can occur in a degenerating meniscus. Meniscus lesions in young children are predominantly due to acute trauma or congenital meniscus variant such as discoid meniscus. In older children they are a result of accident/sport and in adults, they are more chronic tears that occur because of trauma, degenerative disease, or a combination of both. In adults, medial meniscus tears are often associated with cartilage lesions and/or concomitant ligament damage.[16] Medial and lateral meniscus tears are usually categorized based on the anatomic location of the tear, vascularity of the tissue where the tear occurs, and the tear pattern (radial, longitudinal, horizontal, circumferential,

root lesions, bucket handle, oblique/flap tears, and complex degenerative tears).[16,24] Meniscal root tears are defined as radial tears or an avulsion of the insertion of the meniscus.[25,26] Due to failure of the meniscus to convert axial loads into hoop stresses, these types of injuries alter load sharing and the continuity of circumferential fibers leading to progressive arthrosis-like changes in the knee. Initially, a ramp lesion was defined as a longitudinal tear of the peripheral attachment of the posterior horn of the medial meniscus at the meniscocapsular junction of > 2.5 cm in length. Due to different anatomical locations, there is no current agreement regarding the definition of meniscal ramp lesions. Some authors suggest that ramp lesions are associated with injury to the meniscotibial ligament attachment of the posterior horn of the medial meniscus, while others say it is produced by a tear of the peripheral attachment of the posterior horn of the medial meniscus.[27,28] Patient-reported history of recent trauma or prior injury followed by symptoms of meniscal injury (instability, locking, effusion, and tibiofemoral joint line pain) as well as physical examination of the knee (joint line tenderness, effusion, and limitation of range of motion) allows for diagnosis of a meniscal tear.[15,29]

Treatment algorithm of meniscus lesions has evolved tremendously in recent years (►**Fig. 1**). The decision as to whether conservative nonsurgical treatment should be preferred to surgical treatment is highly dependent on the size, pattern, and location of the tear; the patient's age, health status, and activity level; and the surgeon's experience.[16] Although a considerable number of patients having traumatic or degenerative meniscus lesions are treated nonoperatively, meniscus lesions that seem to be mechanically unstable, complex tears, and mostly degenerative meniscus lesions that are symptomatic are often removed by meniscectomy.[24] Arthroscopic partial meniscectomy (APM) is still the most frequent orthopaedic procedure in orthopaedic surgery, although there is evidence that more conservative treatments should be preferred as the first-line treatment when not associated with an acute tear, such as with an ACL tear.[30–33]

Indications for meniscus repair include symptoms directly attributable to the tear, reducibility of the tear, good tissue integrity, and favorable tear characteristics (e.g., single vertical) in one plane in the red–red (R-R) or red–white (R-W) zones of the meniscus or when an ACL is reconstructed.[15,29,34] The following tears are generally considered less amenable for repair: chronic tears with plastic deformity, complete tears with oblique, horizontal cleavage, or complex degenerative pattern in the W-W zone of the meniscus.[29,34,35] Longitudinal tears < 10 mm are often stable and are therefore often left untreated. Incomplete radially oriented tears that do not extend into the outer periphery are less likely to heal and are often left untreated or treated by debridement of the unstable edges. Repair of a radial tear to the periphery is usually encouraged to reduce the risk of having a nonfunctional meniscus. The presence of either untreated instability or OA is also a contraindication for meniscus repair. It has been demonstrated that meniscus repair at the time of ACLR is highly correlated with superior healing rates over "isolated" meniscus tear repairs.[15]
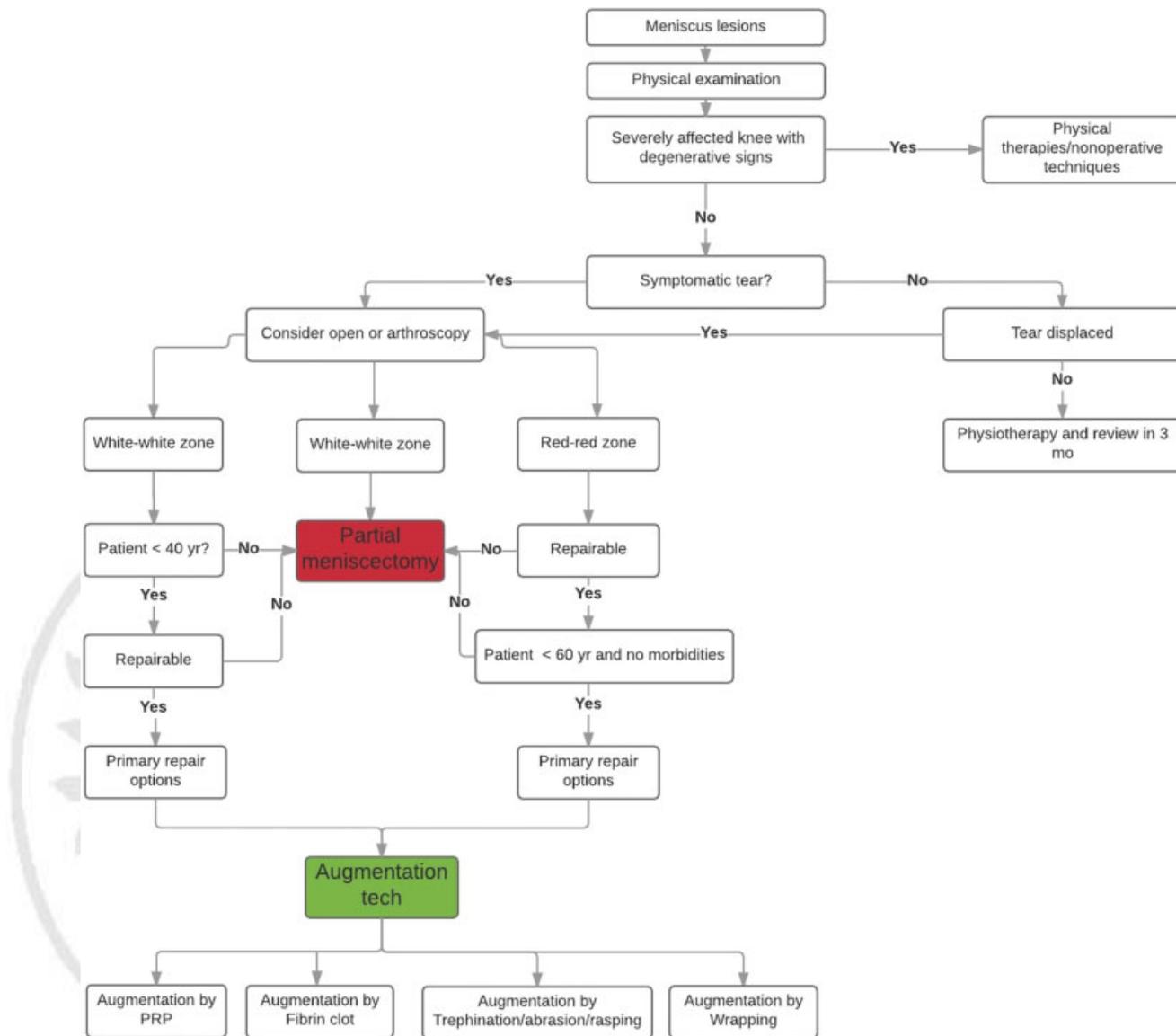
Fig. 1 Treatment algorithm of meniscus lesions. (Adapted from Mordecai et al, 2014.[110])

Recently, there has been a shift toward attempting repair of tears previously deemed irrepairable since preservation of the meniscus structure is expected to maintain meniscus function and prevent degenerative changes to the joints.[16] Satisfactory results have been reported for repair of some horizontal cleavage tears[36] and radial tears,[37] for tears extending into the avascular portion of the meniscus[38] and for patients 40 years and older at the time of surgery.[39] Rehabilitation after meniscus repair surgery usually begins with early active range of motion and restoration of strength exercises, followed by a return to low-impact daily activity within 1 month and return to sports usually at 4 to 6 months, when appropriate functional goals are reached and the patient no longer has point tenderness over the repair site.[40]

Surgical repair of meniscal tears can be performed with inside–out, outside–in, and all-inside techniques. Tears in the anterior or body of the medial or lateral meniscus are easily accessed with the outside–in technique. For poster-ior tears, the inside–out or all-inside techniques are pre-ferred. Although inside–out techniques with vertical divergent sutures are still suggested to be the "gold standard" for meniscus repair, all-inside techniques have the advan-tages of reduced surgical times, ease of use, and low risk of damage of neurovascular structures[16,34] and comparable healing rates in several studies.[41–45] Early meniscal repair devices such as the meniscal arrows and meniscal screws have been associated with chondral damage and have been gradually replaced by suture-based devices. Recently, the all-inside circumferential compression stitching technique has been developed for tears that are difficult to treat with traditional all-inside techniques.[46] Level I and Level II studies comparing different meniscus repair techniques report failure rates between 9 and 43% and anatomic healing rates between 65 and 100% (►Table 1). A systematic review of 13 studies reporting the outcomes of meniscal repair at a minimum of 5 years reported a pooled failure rate of 23%

Table 1 Level I and Level II clinical studies of meniscus repair

Study	Design	Inclusion criteria	Type of tear treated	Surgical approach	Sample size (% males)	Mean age (y)	FU rate (%)	Mean FU times (mo)	Outcome measures	Definition of failure	Results
Bryant et al (2007)[41]	Level I Randomized controlled trial	Patients with a reducible vertical meniscal tear > 10 mm in length and not > 3 mm displaced into the joint in the R-R, or R-W zone that was amenable to repair using sutures or arrows	Vertical tears in the R-R or R-W zone	(1) All-inside with meniscus arrows (n = 51) (2) Inside-out (n = 49) Synovial abrasion 65% with concomitant ACL reconstruction	100 (62)	25	86	28	Retear rate WOMET ACL QofL RofM	Retear was determined by repeat arthroscopic evaluation of patients with follow-up for symptoms of persistent or new pain, catching, or locking that was possibly related to the meniscal repair	Retear rates were 22% for both groups Clinical outcome similar for both groups Operating time longer in Group 2
Kise et al (2015)[11]	Level I Randomized controlled trial	Patients aged 18–40 y with an MRI-verified vertical, longitudinal meniscal tear, 10–40 mm long, located in the peripheral or the middle third of the meniscus, with a preserved central bucket handle eligible for reduction and repair with all-inside technique	Vertical longitudinal tears in the R-R or R-W zone	(1) All-inside with meniscal arrows (n = 21) (2) All-inside with FasT-Fix (n = 25) Rasping of tears 22% with concomitant or earlier ACL reconstruction	46 (57)	26	100 for reoperation 61 for clinical	24	Reoperation rate KOOS Tegner	Reoperation within 2 y as a consequence of complaints due to rerupture or impaired primary healing	Reoperation rates were 43% for Group 1 and 12% for Group 2 (significant) Clinical outcome similar for both groups
Albrecht-Olsen et al (1999)[42]	Level II Randomized controlled trial	Between 18 and 40 y Reliable patients (no abuse) Full-thickness rupture > 10 mm in length Less than 6 mm from the capsule No former ipsilateral meniscus surgery No complex ruptures No arthroscopic arthritis Informed consent prior to surgery	Longitudinal vertical, bucket-handle tears (displaced or in situ) in the R-R or R-W zone	(1) All-inside with meniscus arrows (n = 34) (2) Inside-out (n = 34) Rasping of tears 27% with concomitant ACL reconstruction	68 (81)	26	96	3–4	Second-look arthroscopy Clinical examination	Menisci were defined as healed if there was no residual tear left and as partially healed if there was a residual cleft less than 10 mm and the meniscus was otherwise stable to probing All other arthroscopic cases were defined as nonhealed	91% of patients had healed or partially healed in Group 1 compared with 75% in Group 2 (nonsignificant) Operating time longer in Group 2
Hantes et al (2006)[112]	Level II Randomized controlled trial	Longitudinal full-thickness tear greater than 10 mm in length Location of the tear less than 6 mm from the meniscocapsular junction No former meniscus surgery No evidence of arthritis during arthroscopy Fixation of the meniscus using only one technique (no hybrid fixation)	Longitudinal full-thickness tears in the R-R or R-W zone	(1) Outside-in (n = 17) (2) Inside-out (n = 20) (3) All-inside with RapidLoc (n = 20) Rasping of tears 51% with concomitant ACL reconstruction	57 (77)	27	100	22	Clinical examination IKDC	Using Barrett's criteria, a repaired meniscus was considered healed if there was no joint line tenderness, effusion, and a negative McMurray's test If one or more of these parameters was present, the result was classified as a failure	Healing rates were 100% for Group 1, 95% for Group 2, and 65% for Group 3 (significant) Clinical outcome worst for Group 3 Operating time longer for Group 1
Järvelä et al (2010)[113]	Level II Randomized controlled trial	Traumatic longitudinal unstable meniscal tear in the R-R or R-W zone Less than 6 mo' time delay between the injury and the operation Absence of degenerative meniscal tear or OA of the knee No previous surgery of the knee	Traumatic longitudinal unstable tears in the R-R or R-W zones	(1) All-inside with meniscal screws (n = 21) (2) All-inside with meniscus arrows (n = 21) Rasping of tears 33% with concomitant ACL reconstruction	42 (69)	31	100	27	Clinical examination Lysholm IKDC MRA	Partial meniscal resection at second-look arthroscopy because of persistent knee pain or mechanical symptoms of catching of the knee	Failure rates were 17% for Group 1 and 30% for Group 2 (nonsignificant) Clinical outcome similar for both groups More chondral damage for Group 1

Table 1 (Continued)

Study	Design	Inclusion criteria	Type of tear treated	Surgical approach	Sample size (% males)	Mean age (y)	FU rate (%)	Mean FU times (mo)	Outcome measures	Definition of failure	Results
Barber et al (2005)[43]	Level II Nonrandomized prospective cohort study	Patients with longitudinal meniscal tears in the R-R or R-W zone of the meniscus	Longitudinal tears in the R-R zone (< 3 mm from the synovial meniscal junction) or in the R-W zone (3–5 mm from the synovial meniscal junction)	(1) All-inside with BioStinger (n = 47) (2) Inside–out (n = 29) (3) Hybrid of both (n = 13) Rasping of tear trephination 82% with concomitant ACL reconstruction	85 (64)	27	84	27	Lysholm Tegner Cincinnati IKDC Clinical examination	Identified during second-look arthroscopy due to persistent symptoms	Failure rates were 9% for Group 1, 0% for Group 2, and 15% for Group 3 (nonsignificant) Clinical outcome similar for all groups No chondral damage due to device
Choi et al (2009)[44]	Level II Nonrandomized prospective cohort study	Patients who underwent ACL reconstructions using hamstring tendon autograft combined with repairs of the medial meniscus in a single center by a single surgeon	Longitudinal tears of the posterior horn of the medial meniscus in the R-R or R-W zone with or without additional posterior horn tears of the lateral meniscus	(1) All-inside with sutures (n = 14) (2) Inside–out (n = 34) Rasping of tear 100% with concomitant ACL reconstruction	48 (92)	28	100	36	Lysholm Tegner Lachman Pivot-shift Arthrometer Clinical examination MRI	The meniscus was considered healed if there was no fluid signal within the meniscus on MRI	71.4% of menisci were healed in Group 1 and 70.6% in Group 2 as per MRI Clinical outcome similar for both groups
Spindler et al (2003)[45]	Level II Nonrandomized prospective cohort study	Medial meniscal repairs of the peripheral third or junction of the peripheral third with the middle third performed by the senior surgeon with patellar tendon ACL reconstruction during a certain time period	Longitudinal, bucket-handle and degenerative tears	(1) Inside–out (n = 47) (2) All-inside with meniscus arrows (n = 98) 100% with concomitant ACL reconstruction	145 (55)	24	86	Median 48	KOOS WOMAC SF-36 Lysholm IKDC	Clinical success was defined as no reoperation for failed medial meniscal repair	Failure rates were 18% for Group 1 and 8% for Group 1 (nonsignificant) Clinical outcome similar for both groups Three-y success rates (proportions with no reoperations) were 88% for Group 1 vs. 89% for Group 2
Biedert (2000)[52]	Level II Randomized prospective cohort study	Patients with an isolated and painful medial intrasubstance meniscal lesion, with clinical symptoms of a meniscal tear and a MRI linear high grade 2 signal intensity in the medial meniscus	Isolated and painful medial intrasubstance meniscal lesions	(1) Conservative therapy (n = 12) (2) Arthroscopic suture repair with access channels (n = 10) (3) Arthroscopic minimal central resection, intrameniscal fibrin clot and suture repair (n = 7) (4) Arthroscopic partial meniscectomy (n = 11)	40 (53)	30	100	27	Clinical examination IKDC Radiographs MRI	Not defined	Near-normal or normal findings for 75% patients in Group 1, 90% in Group 2, 43% in Group 3, and 100% in Group 4 (significant)

Abbreviations: ACL, anterior cruciate ligament; FU, follow-up; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Score; MRA, magnetic resonance arthrography; MRI, magnetic resonance imaging; OA, osteoarthritis; QofL, quality of life; RofM, range of motion; R-R, red–red; R-W, red–white; SF-36, Short-Form 36; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; WOMET, Western Ontario Meniscal Evaluation Tool.

with no difference between the different techniques (outside–in, inside–out, or all-inside with arrows).[17] Another systematic review of 27 studies also reported no difference in failures, clinical scores, or complications between inside–out and all-inside repairs (excluding meniscal arrows and screws).[47] In a third systematic review of 31 studies, the authors were unable to determine which all-inside device had the lowest failure rate.[48] A meta-analysis of 21 studies reported a higher failure rate of 16% for all-inside meniscal repair versus 10% for inside–out meniscal repair, both performed concurrently with ACLR.[49] Nerve injuries are associated with inside–out technique and implant-related problems are the most common complications with all-inside technique.[50] In all of the above-mentioned studies, the authors highlighted the present lack of prospective studies with long-term follow-up and the low level of evidence of available data.

Long-term comparisons of meniscus repair versus meniscectomy are scarce and there remains a lack of high-level evidence to guide the surgical management of meniscal tears.[51] A randomized prospective comparative study showed normal or near-normal findings in 100% of patients ($n = 11$) treated with APM versus 90% of patients ($n = 10$) treated with arthroscopic suture repair with access channels at 27 months follow-up.[52] In a retrospective study following 41 patients up to 96 months, failure rates were 14% in the repair group and 10% in the partial meniscectomy group.[53] Clinical outcomes were similar for both groups and no OA progression was noted, but preinjury levels were regained only in the repair group. Another retrospective study compared patients treated with inside–out suturing ($n = 67$) or meniscectomy ($n = 24$) and showed more pain in the latter group.[54] In a retrospective study with 10 years follow-up of 32 patients, Lutz et al (2015) showed higher functional and quality of life scores for repaired vertical lesions in stable knees compared with meniscectomized knees.[55] Radiographic scores were improved for the repaired group suggesting a close correlation between functional and radiographic scores and protective effect of meniscus repair against OA. Finally, recent systematic reviews and meta-analyses concluded that, although meniscus repairs were associated with higher reoperation rate, they result in better long-term patient-reported outcomes and activity levels compared with meniscectomy.[56,57] The Multicenter Orthopaedic Outcomes Network (MOON) prospective longitudinal cohort study reported that a subset of patients treated with meniscus repair at the time of ACLR had an overall failure rate of 14% and significant clinical improvement that was sustained for 6 years.[58]

Augmentation of Meniscus Repair through Trephination, Rasping, and Abrasion

Vascularity of the meniscus is an important determinant for healing.[11,12] The vascular supply of the meniscus is age dependent and the adult meniscus receives vascularity from the perimeniscal capillary plexus, which comes from the superior and inferior branches of the medial and lateral genicular arteries. Multiple preclinical and clinical studies have demonstrated that lesions in the vascular portions of the meniscus with access to the peripheral blood supply have the potential for producing a healing response which is similar to what occurs in other dense fibrous connective tissues during healing, including hemorrhage, proliferation, differentiation, and remodeling. Injuries in the peripheral zones of the meniscus are filled primarily and initially with a highly cellular fibrin clot which acts as a scaffold for repair cells that migrate, proliferate, differentiate, and synthesize repair tissues. Scar tissue remodeling may then take months to mimic the meniscus structure and function. Trephination involves the creation of vascular access channels that run from the vascular portions of the peripheral meniscus toward the more central avascular area to enable bleeding, clot formation, cell migration, and repair. Several preclinical studies have shown that trephination channels enhance the healing of avascular meniscal tears.

Arnoczky and Warren investigated healing response of the meniscus in a dog model at different time points post-injury.[11] The creation of vascular access channels resulted in complete healing of avascular lesions by synthesis of fibrovascular scar tissue which was similar to fibrocartilaginous meniscus tissue after 10 weeks. The healing response appeared to originate from the peripheral synovial tissues. Zhang et al used trephination to treat longitudinal incisions in the avascular area of the meniscus in a unilateral model in dogs and investigated the role of synovial tissues during the healing process.[59] Trephined meniscus repaired first by formation of a granulation tissue which gradually matured into scar tissue. Zhang et al repaired longitudinal meniscus tears located at the avascular portion of the meniscus by suturing and trephination in 20 goats.[60] At 25 weeks post-surgery, 4 out of 20 defects were fully repaired and 16 were partially repaired. The amount, distribution, and organization of collagen bundles were similar to that of normal meniscus, suggesting that repair tissue has the potential to remodel and mature with time. Cook and Fox tested poly-L-lactic acid bioabsorbable conduits designed to maintain trephination channels in surgically created longitudinal avascular meniscus tears in 25 dogs.[61] Treatments with the conduits in conjunction with suturing resulted in functional healing with bridging tissue and biomechanical integrity in 71% of avascular meniscal defects, while no healing was observed with trephination and suturing. Peripheral displacement of the device was commonly observed although neither conduit was completely dislodged into the joint nor articular cartilage damage was noted.

Trephination has also shown some benefits in clinical studies (►**Table 2**). Fox et al repaired symptomatic incomplete meniscus tears (vertical and longitudinal) in 30 patients by using arthroscopic trephination and 90% of patients reported satisfactory to excellent subjective results after 20 months.[62] Zhang and Arnold repaired longitudinal tears by a tooth-like tip trephine device and inside–out arthroscopic horizontal sutures.[63] At an average follow-up of 47 months, seven patients had symptomatic meniscal retear (failure rate of 25%) in the suture group, while two

Table 2 Clinical studies of meniscus repair augmentation by trephination, rasping, and abrasion

Study	Design	Inclusion criteria	Type of tear treated	Surgical approach	Sample size (% males)	Mean age (y)	FU rate (%)	Mean FU times (mo)	Outcome measures	Definition of failure	Results
Zhang and Arnold (1996)[63]	Level III	Patients with longitudinal tears of the white zone at mid-third area from peripheral rim to inner rim of meniscus	Longitudinal tears	(1) Inside–out and trephination (n = 36) (2) Inside–out (n = 28) 95% with concomitant ACL reconstruction	64 (N/S)	22	100	47	Clinical examination	Patients complaining of recurrence of knee swelling and episodes of locking or catching with sign of joint line tenderness, pain with squatting, or positive McMurray's test were considered to possibly have a retear of the meniscus	Failure rates were 6% in Group 1 and 28% in Group 2 (significant)
Shelbourne and Rask (2001)[64]	Level III	Patients with nondegenerative peripheral vertical medial meniscus tears that were deemed salvageable	Peripheral vertical medial meniscus tears > 1 cm in length	(1) Abrasion and trephination (n = 233) (2) Left in situ (n = 139) (3) Inside–out (n = 176) (4) No tear (n = 526) 100% with concomitant ACL reconstruction	548	23	79	Objective 58 Subjective 88	Clinical examination Noyes	Clinical failure of meniscal treatment was described as any patient who required subsequent arthroscopy for meniscal symptoms that required removal or further repair	Failure rates were 6% in Group 1, 10.8% in Group 2, 13.6% in Group 3, and 2.9% in Group 4 (nonsignificant) Group 3 reported more pain and lower activity levels
Shelbourne and Heinrich (2004)[114]	Level III	Patients who had lateral meniscus tears that were left in situ or underwent abrasion and trephination	Posterior horn, radial flap, peripheral, or posterior tears	(1) Abrasion and trephination (n = 43) (2) Left in situ (n = 289) 100% with concomitant ACL reconstruction	332 (57)	23	72	79	Noyes IKDC Radiographs	Subsequent surgery for the lateral meniscus	Failure rate was 2.4% Clinical outcome similar for both groups
Shelbourne et al (2015)[65]	Level III	Patients who had an isolated ACL tear, peripheral vertical nondegenerative medial meniscus tear treated with trephination alone, no lateral meniscus tears, normal radiographs before surgery, and no bilateral knee involvement	Peripheral nondegenerative medial meniscus tears at least 1 cm in length	(1) Trephination (n = 419) (2) No tear (n = 462) 100% with concomitant ACL reconstruction	881	22	69 Objective 85 Subjective	45 Objective 74 Subjective	IKDC Cincinnati	Patients were considered to have a symptomatic medial meniscus tear after surgery when they sought treatment for subsequent injury or disabling symptoms that resulted in a subsequent operation for partial medial meniscectomy	Failure rates were 16.3% in Group 1 and 5.8% in Group 2 (significant) Clinical outcome similar for both groups
Fox et al (1993)[62]	Level IV	Patients who had preoperative subjective and objective findings of a meniscal tear, coinciding with the compartment of the knee with an incomplete meniscal tear, at the time of arthroscopy	Vertical, longitudinal tears that were incomplete	Trephination 17% with concomitant ACL reconstruction	30 (83)	33	97	20	Clinical examination Lysholm	N/S	90% patients reported good to excellent subjective results
Talley and Grana (2000)[70]	Level IV	Patients with partial stable meniscal tears who were treated with parameniscal synovial abrasion at the time of ACL reconstruction	Longitudinal, double longitudinal, and radial	Synovial abrasion 100% with concomitant ACL reconstruction	40 (50)	22	100	40	Clinical examination Arthrometer Tegner Modified AAOS	Failure was defined as a symptomatic meniscal tear requiring subsequent surgery	Failure rate was 11% More failures on the medial side (nonsignificant)
Tetik et al (2002)[69]	Level IV	Patients who had medial joint line pain that interfered with daily living activities	Horizontal tears in the posterior half of the medial meniscus	Rasping of tear Synovial abrasion 0% with concomitant ACL reconstruction	25 (68)	23	100	15	UK-ACL	Excellent result was no pain, no subjective symptoms, full return to sports, no objective pathologic findings	88% patients classified as excellent

(Continued)

Table 2 (*Continued*)

Study	Design	Inclusion criteria	Type of tear treated	Surgical approach	Sample size (% males)	Mean age (y)	FU rate (%)	Mean FU times (mo)	Outcome measures	Definition of failure	Results
Uchio et al (2003)[68]	Level IV	Patients treated by rasping at a particular center during a certain time period	Full-thickness and partial-thickness longitudinal tears	Rasping of tear Synovial abrasion 67% with concomitant ACL reconstruction	47 (42)	24	100	21	Second-look arthroscopy Arthrometer	"No healing" indicated that the tear length had not shortened at the repaired site or a new tear had developed	8% did not heal No effect of age, sex, the time between injury and rasping, the time between rasping and second-look arthroscopy, and concomitant ACL reconstruction on healing Healing better for partial-thickness tears, shorter tears, tears near the capsule, tears in stable menisci

Abbreviations: AAOS, American Association of Orthopaedic Surgeons; ACL, anterior cruciate ligament; FU, follow-up; IKDC, International Knee Documentation Committee; N/S, not specified; UK-ACL, University of Kentucky Anterior Cruciate Ligament test.

patients in the trephination and suture group showed symptomatic meniscal retear (failure rate of 6%). Shelbourne and Rask repaired peripheral vertical medial meniscus tears > 1 cm in length (100% with concomitant ACLR) by using different techniques.[64] Failure rate was 6% for the 233 patients who had undergone abrasion and trephination. Shelbourne and Dersam repaired radial flap tear, posterior horn tear, and peripheral tears in the lateral meniscus using abrasion and trephination or left the tears in situ at the time of ACLR.[54] Overall failure rate was 2.4% at 79 months and clinical outcome was similar for both groups. Shelbourne et al repaired peripheral nondegenerative medial meniscus tears at least 1 cm in length by arthroscopic trephination during ACLR.[65] Failure rate was 16.3% at 5.6-year follow-up and trephination-treated tears showed 95% normal radiographs. However, none of these studies objectively evaluated anatomic meniscus healing using an imaging study or second-look arthroscopy.

Other augmentation techniques involve rasping the meniscal tear and slightly abrading the synovium. Okuda et al surgically created full-thickness longitudinal lesions in the avascular zone, the medial meniscus in a rabbit model and repaired it by rasping on the surface of the meniscus from the parameniscal synovium to the injured portion.[66] Early macroscopic and histological evaluation showed hypertrophic synovial tissue invading the lesion from the parameniscal synovium. Fibrous repair was complete in all layers of the injured portion in the rasped meniscus at 16 weeks. They concluded that rasping of parameniscal synovium without suturing could be an uncomplicated way to augment meniscus healing. Ochi et al created full-thickness longitudinal tears in the avascular zone of the medial menisci in a rabbit model and assessed mechanisms of meniscus healing following rasping of the parameniscal synovium and meniscus surface.[67] Immunohistochemistry showed that the rasped surface stayed highly positive for interleukin-1α, transforming growth factor-β1 (TGF-β1), platelet-derived growth factor (PDGF), and proliferating cell nuclear antigen at 1, 7, 14, and 7 days postsurgery and then gradually declined. They suggested that rasping could stimulate chondrocytes in the meniscus surface area to synthesize specific types of growth factors and cytokines, and such synthesized proteins can stimulate the metabolism of the chondrocytes and attract the synovial tissue with its rich vascularity to the injured site to aid in healing.

Synovial abrasion and rasping have also been applied clinically (►**Table 2**). Uchio et al treated full-thickness and partial-thickness longitudinal tears in 47 patients by rasping the tear and synovial abrasion.[68] Healing rate was a reported 92%. They found no effect of age, sex, time between injury and rasping, time between rasping and second-look arthroscopy, and concomitant ACLR on the healing rate. However, healing was better for partial-thickness tears, shorter tears, tears near the capsule, and tears in stable menisci. Tetik et al reported repairing horizontal tears in the posterior half of the medial meniscus in 25 patients by rasping of the tear and synovial abrasion.[69] After 15 months follow-up, 88% of the patients were classified as excellent (no pain, no subjective symptoms, full return to sports, no objective pathologic findings). Talley

and Grana repaired longitudinal, double longitudinal, and radial tears in 40 patients by synovial abrasion at the time of ACLR.[70] Overall failure rate was 11% (4% for lateral meniscus and 21% for medial meniscus) at 3.3-year follow-up.

All of the earlier studies indicate that trephination, rasping, and abrasion are easy treatment modalities that can contribute to meniscus repair. In fact, these augmentation techniques are often used in conjunction with outside–in, inside–out, or all-inside repair (►Table 1). One potential drawback of trephination is that the trephination channels may damage the peripheral circumferential fibers and have adverse effects on the biomechanical properties of the meniscus. In addition, self-collapse and channel closure could lead to blocked cell migration. Furthermore, it is still not known whether a single large or multiple small channels are more efficient for meniscus healing. One limitation of synovial abrasion and rasping is that they appear to be less efficient in repairing tears that are far from the capsule.

Augmentation of Meniscus Repair with Fibrin/Blood Clots

Meniscus healing is a complex process that is associated with many cellular and molecular events, including hemorrhage, clot formation, granulation, vascularization, cell ingrowth, cell infiltration, ECM synthesis, scar tissue formation, and scar remodeling. Depending on the lesion location and size, healing processes may differ. The wound hematoma contains a spectrum of PDGFs as well as clot components which are chemotactic and are expected to promote proliferation and differentiation of cells. Fibrin glue, exogenous fibrin clots, and in situ forming fibrin clots have all been used in preclinical and clinical studies to augment meniscus repair. Microfracture of the intercondylar notch was also introduced to enhance the repair of isolated meniscus tears by inducing blood and bone marrow (BM) elements into the joint.[71] Although the exact mechanisms of action of fibrin clots have not been completely elucidated at this point, they appear to have the potential to accelerate tissue healing in meniscus.

Ishimura et al[72] surgically created full-thickness lesions in avascular areas on the anterior segment of the medial meniscus in a rabbit model. Autologous plasma-derived fibrin glue used in conjunction with BM cells (BMC) accelerated histological maturation of the repair tissue and improved repair compared with the acellular fibrin glue by itself at 12 weeks. Ishimura et al[73] arthroscopically repaired 40 meniscal tears in 32 patients using purified fibrin glue. At 3 years follow-up, two patients had recurrence of meniscal symptoms and underwent partial meniscectomy. Second-look arthroscopic evaluation rated 20 out of 25 repairs as good (80%), 4 as fair, and 1 as poor. In another study, Ishimura et al[74] used purified fibrin glue to repair 61 menisci in 40 patients. The rate of recurrence of tears in the R-R zone or R-W zone was 10% at an average follow-up of 8 years, whereas it was 17% for tears in the W-W zone. Second-look arthroscopy in 27 patients revealed that 77% of repairs were considered good, 11.5% fair, and 11.5% poor. In the study by Arnoczky and Warren,[11] implantation/placement of exogenous fibrin clot into stable full-thickness defects in the avascular medial portion of meniscus in dogs improved the healing response via proliferation of fibrous connective tissue, which gradually remodeled into fibrocartilaginous tissue. Filling the lesion area with a fibrin clot provided a scaffold matrix and secretion of mitogenic components to recruit cells that probably originated from the adjacent meniscal tissue and synovial membrane.

Ritchie et al surgically created unilateral peripheral longitudinal tears in the meniscus in a goat model to assess the effect of two different adjunctive healing techniques.[75] Goats in Group I received inside–out horizontal mattress sutures, goats in Group II received inside–out sutures plus placement of an exogenous fibrin clot inside the defect as a healing enhancer, and goats in Group III received inside–out sutures, rasping, and synovium abrasion. Healing rates were 100% in Group I, 17% in Group II, and 87.5% in Group III, which suggests that the use of the adjuncts was not necessary. Port et al[76] surgically created a full-thickness lesion in avascular zones of the meniscus in a goat model and assessed application of fibrin clot and autologous cultured adherent BMC in the site of the defect by histology and mechanical testing. In this case, administration of cultured BM-derived cells in combination with exogenous fibrin clot failed to improve meniscal healing by 16 weeks. Nakhostine et al[77] created 5 to 7 mm longitudinal full-thickness incisions in the avascular portion of the meniscus in an ovine model, which were further injected with 3 mL of blood clot through a trephination channel running from the periphery of the meniscus to the mid portion of the lesion. The addition of exogenous blood clot in this model without additional stabilization was not sufficient to promote complete healing of torn menisci.

Fibrin/blood clots have also been used clinically (►Table 3). van Trommel et al treated five patients who had a tear of the posterolateral aspect of the lateral meniscus with suturing and placement of an exogenous fibrin clot in the seam of the tear.[78] Healing was complete for the three patients who were available for follow-up. The authors suggested that application of an exogenous fibrin clot might improve healing of tears located in the avascular portion of the meniscus. Biedert compared the effect of four different methods, including conservative therapy ($n = 12$), arthroscopic suture repair with channels ($n = 10$), arthroscopic central resection and intrameniscal administration of fibrin clot by suture repair ($n = 7$), and APM ($n = 11$), for treatment of isolated and symptomatic painful horizontal grade 2 meniscal lesions (intrasubstance meniscal lesions) on the medial side in 40 patients.[52] Only 43% of the patients treated with administration of fibrin clot had normal or near-normal evaluation at follow-up. Jang et al[79] reported a novel method for delivering fibrin clots to the target area of meniscal tear by arthroscopic technique to augment the rate of healing. In this technique, the sutured fibrin clot is passed through a plastic transparent shoulder cannula to the desired location by pulling off the needle. They reported a success rate of 95%. Ra et al[80] used fibrin clot as an alternative effective method for treatment of complete radial tear of meniscus by arthroscopic inside–out repair suturing in 12 patients. They found improved clinical scores and complete

Table 3 Clinical studies of meniscus repair augmentation by fibrin/blood clots

Study	Design	Inclusion criteria	Type of tear treated	Surgical approach	Sample size (% males)	Mean age (y)	FU rate (%)	Mean FU times (mo)	Outcome measures	Definition of failure	Results
Biedert (2000)[52]	Level II Randomized prospective cohort study	Patients with an isolated and painful medial intrasubstance meniscal lesion, with clinical symptoms of a meniscal tear and a MRI linear high grade 2 signal intensity in the medial meniscus	Isolated and painful medial intrasubstance meniscal lesions	(1) Conservative therapy (n = 12) (2) Arthroscopic suture repair with access channels (n = 10) (3) Arthroscopic minimal central resection, intrameniscal fibrin clot and suture repair (n = 7) (4) Arthroscopic partial meniscectomy (n = 11)	40 (53)	30	100	27	Clinical examination IKDC Radiographs MRI	Not defined	Near-normal or normal findings for 75% patients in Group 1, 90% in Group 2, 43% in Group 3, and 100% in Group 4 (significant)
Ishimura et al (1991)[73]	Level IV	Patients who had arthroscopic meniscal repair using fibrin glue	Longitudinal and bucket-handle tears	Fibrin glue Reduction with suturing in unstable tears	32 (25)	18	63 for second-look arthroscopy	46 6 for second-look arthrocopy	Second-look arthroscopy	Patients complained of meniscal symptoms	Failure rate was 6% 20 repairs rated as good, 4 as fair, and 1 as poor by arthroscopic evaluation criteria
Ishimura et al (1997)[74]	Level IV	Patients who had arthroscopic meniscal repair using fibrin glue	Longitudinal and bucket-handle tears in all zones	Fibrin glue Reduction with suturing in the case of unstable tears Rasping of tear 84% with concomitant ACL reconstruction	40 (33)	20	68 for second-look arthroscopy	96 10 for second-look arthro-scopy	Second-look arthroscopy	Patients complained of meniscal symptoms and received partial meniscectomy	Failure rate was 15% 77% repairs rated as good, 11.5% fair, and 11.5% poor by arthroscopic evaluation criteria Recurrence of meniscal symptoms correlated with insufficiency of the reconstructed ACL, repair of fresh tears, and repairs requiring supplementary meniscal sutures
van Trommel et al (1998)[78]	Level IV	Patients that had complete radial split at the level of the popliteus fossa extending from the periphery to the central part of the lateral meniscus	Radial tears	Outside-in Exogenous fibrin clot Rasping of tear 20% with concomitant ACL reconstruction	5 (N/S)	20	60	71	Second-look arthroscopy MRI	Meniscus was deemed to be healed if there was no fluid imbibition into the substance of the fibrocartilage on MRI	All cases healed
Kamimura and Kimura (2011)[81]	Level IV	Patients who had horizontal cleavage tears with meniscal degeneration	Horizontal cleavage tears	All-inside with FasT-Fix Exogenous fibrin clot	9 (N/S)	N/S	100	12	Second-look arthroscopy	N/S	Cleft had closed and had healed with a layer of vascular synovial tissue extending over the proximal surface of the lateral meniscus
Kamimura and Kimura (2014)[82]	Level IV	Patients who had a horizontal cleavage tear associated with degeneration identified using MRI and arthroscopy Clinical findings limited to	Horizontal cleavage tears	All-inside with FasT-Fix Exogenous fibrin clot 17% with concomitant ACL reconstruction	18 (60 for second-look arthroscopy)	36	56	41 7 for second-look arthro-scopy	Lysholm IKDC Tegner Second-look arthroscopy	N/S	Complete healing in 70% of patients as assessed by arthroscopy

Table 3 (Continued)

Study	Design	Inclusion criteria	Type of tear treated	Surgical approach	Sample size (% males)	Mean age (y)	FU rate (%)	Mean FU times (mo)	Outcome measures	Definition of failure	Results
		a positive McMurray's test or pain during movement, especially in full flexion; Tenderness of the femorotibial joint line; No limitation of range of motion									
Jang et al (2011)[79]	Level IV	Patients who had a radial tear that was deemed repairable	Radial, longitudinal in R-W zone, transverse and oblique tears	Suturing, Exogenous fibrin clot, Rasping of tear, Synovial abrasion	41 (N/S)	N/S	100	8	Second-look arthroscopy, MRI	N/S	Failure rate was 5%
Ra et al (2013)[80]	Level IV	Patients who had complete radial tears of the meniscus	Radial tears	Inside–out, Exogenous fibrin clot, Rasping of tear, Synovial abrasion, 17% with concomitant ACL reconstruction	12 (92)	N/S	100	30, 11 for MRI	IKDC, Lysholm, MRI, Second-look arthroscopy	N/S	Complete healing in 92% patients on MRI

Abbreviations: ACL, anterior cruciate ligament; FU, follow-up; IKDC, International Knee Documentation Committee; MRI, magnetic resonance imaging; N/S, not specified; R-W, red–white.

healing in most patients on follow-up magnetic resonance imaging and second-look arthroscopy. Horizontal cleavage tears with meniscal degeneration indications are difficult to heal.[36] Kamimura and Kimura showed functional joint improvement and meniscal healing in patients with horizontal cleavage tear with meniscal degeneration (difficult-to-treat injuries) treated with FasT-Fix (Smith and Nephew) vertical sutures and placement of exogenous fibrin clots within the cleft.[81] At 12 months follow-up, they[82] showed 70% complete healing rate and improvement of Lysholm, International Knee Documentation Committee subjective scores, and Tegner activity level. They suggested that this technique could be considered as a treatment option for younger patients with a stable knee with a degenerative horizontal cleavage tear. To biologically augment repair of meniscal tears, Sethi et al developed a simple intra-articular technique to deliver blood clots by abrading the synovium and allowing the blood to run down the synovial wall and into the meniscal cleft, pooling there and forming a clot adherent to the edges of the separated meniscal tear close to the tear site.[83] The authors claimed that their technique has a few advantages over using the exogenous fibrin clot such as being simple, easy to handle, safe, minimally invasive (does not depend on exogenous preparation), does not require the assistance of operating room staff, and does not add a significant amount of time to the meniscal repair.

Although using fibrin/blood clots in the context of meniscal repair has yielded equivocal and conflicting results in preclinical and clinical settings, this remains a simple and easy option to potentially augment healing in the setting of meniscus repair. Further high-level evidence is still required.

Augmentation of Meniscus Repair with Platelet-Rich Plasma

PRP is currently used in the sports medicine and orthopaedics fields to treat different conditions such as tendinopathy or OA.[84,85] PRP contains various types of growth factors including PDGF, TGF-β, vascular endothelial growth factor, epidermal growth factor, insulin-like growth factor-I, fibroblastic growth factor, and hepatocyte growth factor. In theory, using PRP to augment meniscus repair appears to be reasonable. Although some orthopaedic surgeons have incorporated PRP for meniscus repair in their practice, preclinical and clinical data are still lacking. In addition, much of the difficulty in interpreting the effects of PRP is the documented variability of the contents of each specific preparation and that PRP is not a uniform product.

In a study by Ishida et al,[86] a gelatin hydrogel scaffold was used as a drug delivery system for growth factors secreted by PRP to enhance the healing of meniscal defects in a rabbit model. The combination of gelatin–PRP was compared with two other groups including platelet-poor plasma and control for the intervals of 4, 8, and 12 weeks. Their findings suggested that the combination of hydrogel and PRP supports meniscal cell proliferation and the synthesis of an extracellular matrix, which is rich in glycosaminoglycan. In addition, they found greater messenger RNA expression of biglycan and decorin. Zellner at al[87] created a circular 2-mm punch meniscal defect

in the avascular zone of rabbit meniscus which was then either left empty or treated with biodegradable hyaluronan–collagen composite matrices loaded/seeded with PRP, BM, BM/mesenchymal stem cells (MSC) precultured in chondrogenic medium (CM) for 2 weeks or BM/MSC without any preculture. Their findings illustrated that MSCs appear to be necessary for meniscal healing in repair of punch defect model in rabbit. In line with their previous findings, Zellner et al[88] showed seeding of MSC on biodegradable hyaluronan–collagen composite matrices, which were precultured in CM produced/generated extensive and organized matrix mimicking native meniscus by better biomechanical integration after 12 weeks of histological/mechanical assessment. In both of the earlier studies, the groups treated with hyaluronan–collagen composite matrices and PRP did not do better than the empty controls. In another study, Shin et al[89] compared the effect of leukocyte-rich PRP (L-PRP) on healing of the horizontal medial meniscus tears in a rabbit model. The horizontal tear (6 mm in width and 1.5 mm in length) were created in the anterior horn of the medial meniscus and were either injected with L-PRP or left untreated. Histological findings revealed there were no significant differences in quantitative histologic scoring between the two groups at 2, 4, and 6 weeks after surgery. Lee et al[90] created 2-mm full-thickness circular defects in the anterior portion of the inner two-third of the avascular zone of the medial meniscus in rabbits which were filled with fibrin glue or 10% PRP. Upon retrieval after 8 weeks, the lesions in both the control and PRP groups were filled with fibrous and fibrillated connective tissue and did not show any meniscal cartilage formation.

To our knowledge, there are only a few clinical studies that use PRP application for treatment of meniscal lesions (►Table 4). Pujol et al[91] used PRP to augment repair and promote meniscal healing of horizontal cleavage meniscal tears repaired with an open approach. In this case–control study, 34 young patients underwent either a standard open meniscal repair ($n = 17$) or the same surgical repair with introduction of PRP in the lesion ($n = 17$). They found that clinical outcome was slightly improved in the PRP group. Griffin et al[92] performed 35 isolated arthroscopic meniscus repairs, 15 of which were augmented with PRP. In contrast to the above-mentioned study, they showed that outcome was similar after meniscus repair without and with PRP. The authors stated that an appropriate larger sample size is needed to elucidate the beneficial effect of PRP.

Augmentation of Meniscus Repair by Wrapping

Meniscus wrapping techniques were first described by Henning et al who used fascial sheath coverage and exogenous fibrin clot to treat meniscal tears[93,94] (►Table 5). The fibrin clot was believed to act as a scaffold and also provide chemotactic and mitogenic factors and stimuli to assist the reparative process. The authors' stated opinion was that the fascia sheath worked by partially encapsulating the meniscus and decreasing the effect of early washout of the exogenous clot injection.[94] The surgical technique involved rasping of the parameniscal synovium, peripheral white rim, and tear surface of the fragment. The meniscus itself was sutured using inside–out technique and then a fascia sheath taken from the distal anterolateral thigh was sutured over the meniscus to cover the repair. Finally, an exogenous fibrin clot was injected under the sheath. Complex tears including double flap, double longitudinal and radial tears all showed improved healing with the addition of the sheath and fibrin clot.[93] Complete or partial healing was seen in 26 of the 31 repairs treated with this technique.[94] However, this technique is considered inadequate for radial tears in the middle portion of the middle one-third of the lateral meniscus.[94] This technique also has the disadvantage of being technically demanding and time-consuming. In 1996, Barrett and Treacy reported that Henning et al's technique had not been widely adopted partly due to the technical difficulty in securing the sheath around the repaired meniscal tear.[95] Then, they described repair of complex tears in the medial and lateral menisci that involved combining T-fix (Acufex) and inside–out approaches as an improvement to the original technique. The technique consisted of rasping the synovium and the tear, inside–out repair of the meniscus, anchoring and suturing of the fascial sheath using T-fix, and inside–out sutures, as well as injection of a blood clot under the sheath. They concluded that this technique was much easier than that previously described and suggested that it could be used to improve repair of complex tears.

Jacobi and Jakob have been advocating for many years for treating complex human meniscal tears, which otherwise would have a poor clinical probability of healing, with a collagen wrap as an adjunct. This meniscus wrapping technique was introduced in 2003 and first used to treat 30 patients who had complex tears, delayed traumatic tears with degenerative aspects, or repeat sutured tears, all in the R-W or W-W zone.[96] In this study, 15 complex tears, 11 bucket-handle and 4 horizontal tears were treated with this technique. The tears in the meniscus were first fixed by preliminary inside–out sutures. Chondro-Gide matrix (Geistlich Pharma) was then introduced through an arthroscopic cannula and multiple sutures were added (up to 10), to complete the fixation of the membrane on the meniscus and the meniscus tear. The porous layer was laid down facing the meniscal defect to favor cell invasion and attachment and allow the in-growth of cells and a newly formed tissue. The compact layer acts as occlusive scaffold with smooth surface to prevent cells from diffusing into the synovial fluid. Three patients had a symptomatic failure (10%) at mean follow-up of 2.5 years, while all other 27 cases (90%) were asymptomatic. It is believed that the membrane acts as an internal bioreactor or scaffold and attracts cells that are released from the synovial fluid by rasping and bleeding inside the joint. Thus, healing becomes possible even in unfavorable conditions with this technique. Similar to the fascial sheath technique, this procedure is technically demanding and time-consuming.

Meniscus wrapping with a cross-linked Chondro-Gide derivative was similarly used in a preclinical study in a goat model.[97] Surgically induced 6-mm horizontal tears in the avascular portion of the meniscus were closed with a

Table 4 Clinical studies of meniscus repair augmentation by platelet-rich plasma

Study	Design	Inclusion criteria	Type of tear treated	Surgical approach	Sample size (% males)	Mean age (y)	FU rate (%)	Mean FU times (mo)	Outcome measures	Definition of failure	Results
Griffin et al (2015)[92]	Level III	Patients who underwent arthroscopic meniscus repair during a particular period at one center and were older than 18 years	Bucket handle and horizontal, peripheral horizontal, peripheral longitudinal, horizontal, longitudinal at R-W junction, longitudinal, bucket-handle, vertical and undersurface tears	Inside–out All-inside Outside–in Application of Cascade PRF delivered arthroscopically and sutured into the repair site using a PDS suture 0% with concomitant ACL reconstruction	35 (80) 15 with PRP 20 without PRP	31	100	48	IKDC Tegner-Lysholm Return to sport Return to work RofM	Known recurrence of reoperation	Failure rates were 27% in PRP + group and 25% in PRP − group Clinical outcome similar for both groups
Pujol et al (2015)[91]	Level III	Patients younger than 40 years with a symptomatic horizontal cleavage (grade 2 or 3) of the meniscus and persisting pain after complete medical treatment (rest, physiotherapy, intra-articular injections of corticosteroids) for at least 6 mo	Horizontal cleavage tears extending into the avascular zone	Open suturing Injection of GPSIII PRP directly into the repair lesion prior to closure Rasping of tear 0% with concomitant ACL reconstruction	34 (71) 17 with PRP 17 without PRP	30	100	32	KOOS IKDC MRI	Failure was defined as a reoperation on the same knee for a meniscectomy or an iterative repair of the same meniscus	Failure rates were 5.8% in PRP + group and 11.8% in PRP − group Clinical outcomes were slightly improved by the addition of PRP (pain and sports activity subcategories)

Abbreviations: ACL, anterior cruciate ligament; GPSIII, gravitational platelet separation system III; FU, follow-up; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Score; MRI, magnetic resonance imaging; PRF, platelet-rich fibrin; PDS, polydioxanone; PRP, platelet-rich plasma; RofM, range of motion; R-W, red–white.

Table 5 Clinical studies of meniscus repair augmentation by wrapping

Study	Design	Inclusion criteria	Type of tear treated	Surgical approach	Sample size (% males)	Mean age (y)	FU rate (%)	Mean FU times (mo)	Outcome measures	Definition of failure	Results
Henning et al (1990)[93]	Level IV	Patients aged 14–45 y with unstable torn meniscus who underwent repair during a particular period	Single longitudinal, double longitudinal, triple longitudinal, radial, flap, horizontal split, and bucket-handle tears	Rasping of tear Suturing Wrapping with fascial sheath Exogenous fibrin clot 92% with concomitant ACL reconstruction	153 (N/S)	23	100	4	Arthrogram Second-look arthroscopy	Healing over less than 50% of the vertical height was considered a failure	Failure rate was 12% Failure rate greater for complex tears Exogenous blood clots decreased failure rate in isolated tears (41–8%) Exogenous blood clots with fascial sheath decreased failure rate in complex tears (22–11%)
Henning et al (1991)[94]	Level IV	Patients with unstable complex tears that underwent repair during a particular period	Double longitudinal, double flap and radial tears	Rasping of tear Suturing Wrapping with fascial sheath Exogenous fibrin clot 81% with concomitant ACL reconstruction	31 with sheath (N/S) 58 without sheath in previous series (N/S)	N/S	100	6 to 9	Arthrogram Second-look arthroscopy	Healing over less than 50% of the vertical height was considered a failure	Failure rates were 8% with sheath and 24% without sheath
Jacobi and Jakob (2010)[96]	Level IV	Patients with tears in the R-R or R-W zone, complex tears, delayed traumatic tears with degenerative aspects, or repeat sutures	Complex, bucket-handle, and longitudinal tears	Inside–out Wrapping with collagen matrix 33% with concomitant ACL reconstruction	30 (63)	N/S	100	30	Clinical examination	Persistence of symptoms	Failure rate was 10%
Piontek et al (2016)[99]	Level IV	Full thickness, combined meniscal tear greater than 20 mm in length Horizontal and radial tear Tear location reaching more than 6 mm from the meniscocapsular junction including the avascular zone Both degenerative and nondegenerative menisci (i.e., horizontal and radial tears, involving the W-W and R-W zone, as well as extensive tears of the bucket-handle type)	Combined (horizontal and radial or longitudinal component) and complex meniscal tears (tear extended through avascular zones or/and composed of two or more morphological tear pattern)	All-inside with FasT-Fix Wrapping with collagen matrix 40% with concomitant ACL reconstruction	53 (75)	37	94	24	IKDC Lysholm Barret MRI WORMS	Failure if at the follow-up process patient underwent partial/complete meniscectomy or knee replacement	Failure rate was 4% Clinical outcome improved in 86.8% of the intended to treat cases Nonhomogeneous signal without meniscal tear in 76% of cases on MRI (WORMS grade 1)

Abbreviations: ACL, anterior cruciate ligament; FU, follow-up; IKDC, International Knee Documentation Committee; MRI, magnetic resonance imaging; N/S, not specified; R-R, red–red; R-W, red–white; W-W, white–white; WORMS, Whole Organ MRI Score.

single suture introduced with the inside–out technique. The menisci were then wrapped with a collagen membrane and fibrin glue was used to seal the membrane (as a tissue adhesive). In some animals, meniscus wrapping was combined with injection of expanded autologous chondrocytes. Meniscus wrapping by itself improved healing at 3 months compared with suturing alone, but this improved outcome was not observed at the 6-month repair period. Combining the meniscus wrapping and autologous chondrocyte injections improved repair at both 3 and 6 months time points.

In 2012, Piontek et al reported on the development of a fully arthroscopic wrapping technique to treat meniscal lesions.[98] This arthroscopic method combines suturing techniques with the use of a collagen membrane to wrap the meniscus and the optional application of BM aspirate or concentrate deep to the membrane. In this technique, the tears were first sutured with all-inside FasT-Fix sutures (Smith and Nephew). The meniscus was then wrapped with collagen matrix and BM aspirated from the tibial proximal epiphysis was injected under the matrix into the tears. The authors stated that the technique was technically challenging, but they believed that the use of collagen matrix and addition of BM aspirate will create favorable conditions, which may increase the rate of meniscus healing. The 2-year follow-up data of tears treated with arthroscopic suturing and wrapping technique were presented in a subsequent article.[99] Inclusion criteria for this study included full-thickness tears greater than 20 mm in length, horizontal, radial tears, and extensive bucket-handle tears, tears located at greater than 6 mm from the capsular junction including the avascular zone, as well as both degenerative and nondegenerative menisci. Of the 48 cases analyzed, only 2 patients underwent subsequent partial meniscectomy and were considered failures. Subjective and clinical assessment scores were improved at 2 years postoperative in the patients. The authors reported 13 severe adverse events but specified that none of the events was related to the procedure or material used. They concluded that this technique is safe and promising and can be used by surgeons to repair menisci which would otherwise be removed.

Rationale for Using Polymer Stabilized PRP to Augment Meniscus Repair

Chitosan is a positively charged partially acetylated glucosamine-based polysaccharide that can act as a scaffold and adhere to negatively charged tissue surfaces to mediate tissue repair. Near-neutral solutions of chitosan–glycerol phosphate (GP) can be mixed with whole blood to create hybrid clots[100] that significantly resist retraction.[101] We have previously demonstrated that chitosan–GP/blood clots can be injected over marrow stimulated cartilage defects and yield repair tissues with improved biomechanical and biochemical properties compared with microfracture or microdrilling alone.[101,102] Some of the mechanisms responsible for this improved repair are an increase in inflammatory and marrow-derived stromal cell recruitment to the microdrill holes; increased vascularization and subchondral bone remodeling at early postsurgical time points from day 1 and 56 days when

compared with microdrilled control holes[103]; polarization of macrophage phenotype toward the alternatively activated prowound healing lineage[104]; increased bone remodeling and osteoclast activation leading to better repair tissue integration[105]; and stimulated secretion of anabolic wound repair factors from M2a macrophages.[106]

Recently, we have developed freeze-dried formulations of chitosan that can be solubilized in PRP to form injectable implants that solidify in situ.[107] These freeze-dried formulations contain chitosan, a lyoprotectant and a clot activator. We found that chitosan molecular size, chitosan concentration, and lyoprotectant concentration control the performance characteristics of these implants and have identified formulations that show promise for meniscus repair. In two pilot studies,[108,109] meniscus repair in ovine models was improved by application of freeze-dried chitosan–PRP implants. Chitosan–PRP implants induced cell recruitment to the tears, repair tissue synthesis, and remodeling at 3, 6 weeks, and 3 months postsurgery leading to the design of an ongoing pivotal animal study. Chitosan–PRP implants may be able to overcome some of the shortcomings of current augmentation techniques to improve restoration of meniscus structure and function.

Conclusion

Meniscus tears are among the most common knee injuries related to trauma or aging. Understanding of the structure, vascularity, biomechanics, and pattern of tears is important and could facilitate the orthopaedic surgeon's selection of optimal treatment. Current trends are shifting toward salvaging the meniscus tissue and meniscus repair with good to fair satisfactory long-term outcome. Evidence shows that nonsurgical approaches/management can be successful especially in the short term if tears are not symptomatic. Diverse augmentation techniques have been developed to introduce marrow elements and blood components into the joint to increase healing in the avascular zone of the meniscus. Further development of these approaches and bioactive materials may improve repair of currently irreparable meniscus tears.

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