

Labral Reconstruction via Capsular Augmentation Maintains Perfusion to the Acetabular Labrum and Locally Transferred Autograft

An in Vivo Laser Doppler Flowmetry Analysis

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Background: The purpose of the present study was to examine the effects of arthroscopic labral repair with capsular augmentation on blood flow in vivo with use of laser Doppler flowmetry (LDF) to measure microvascular perfusion of the labrum and autograft tissue.

Methods: The present prospective case series included patients ≥ 18 years old who underwent arthroscopic acetabular labral repair with capsular augmentation; all procedures were performed by a single surgeon between 2018 and 2022. The LDF probe measured microvascular blood flow flux within 1 mm^3 of the surrounding labral and capsular tissue of interest. Mean baseline measurements of flux were compared with readings immediately following capsular elevation and after completing labral augmentation. Blood flux changes were expressed as the percent change from the baseline measurements.

Results: The present study included 41 patients (24 men [58.5%] and 17 women [41.5%]) with a mean age (and standard deviation) of 31.3 ± 8.4 years, a mean BMI of $24.6 \pm 3.4 \text{ kg/m}^2$, a mean lateral center-edge of angle $35.3^\circ \pm 4.9^\circ$, a mean Tönnis angle of $5.8^\circ \pm 5.8^\circ$, and a mean arterial pressure of $93.7 \pm 10.9 \text{ mm Hg}$. Following capsular elevation, the mean percent change in capsular blood flow flux was significantly different from baseline (-9.24% [95% confidence interval (CI), -18.1% to -0.04%]; $p < 0.001$). Following labral augmentation, the mean percent change in labral blood flow flux was significantly different from baseline both medially (-22.3% [95% CI, -32.7% to -11.9%]; $p < 0.001$) and laterally (-32.5% [95% CI, -41.5% to -23.6%]; $p = 0.041$). There was no significant difference between the changes in medial and lateral perfusion following repair ($p = 0.136$).

Conclusions: Labral repair with capsular augmentation sustains a reduced blood flow to the native labrum and capsular tissue at the time of fixation. The biological importance of this reduction is unknown, but these findings may serve as a benchmark for other labral preservation techniques and support future correlations with clinical outcomes.

Level of Evidence: Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.

The acetabular labrum is crucial for maintaining the proper physiological function of the hip joint by facilitating negative intra-articular pressure (i.e., a suction seal) between the femoral head and the acetabulum¹⁻⁵. Labral tears disrupt this physiological fluid seal and contribute to the acceleration of cartilage layer consolidation^{4,6}. While partial debridement/resection

may provide interim symptom relief, multiple studies have suggested that labral repair, augmentation, and reconstruction may offer more favorable long-term outcomes and survivorship in terms of conversion to total hip arthroplasty⁷⁻¹². As a result, an increasing emphasis has been placed on more advanced preservation techniques to reconstitute the suction seal of the hip.

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (<http://links.lww.com/JBJSOA/A556>).

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Although labral repair is usually the preferred method of treatment, surgeons may be challenged when insufficient labral tissue remains for primary repair. In cases involving complex tears, advanced degeneration, or hypoplastic tissue (<5 mm in width), labral augmentation or reconstruction may be necessary to reconstitute the suction seal of the joint. While many techniques of labral reconstruction have demonstrated positive short to intermediate-term outcomes, implantation of graft-to-bone reconstructions requires extensive debridement and labral detachment that inherently compromises the existing blood supply¹³⁻¹⁹. Conversely, labral augmentation preserves the native labral/chondral complex and has been associated with a superior reconstitution of the hip suction seal (i.e., greater force necessary for femoral head displacement) and better integration of soft tissue with the chondral surface²⁰⁻²².

The cadaveric study by Kalhor et al. confirmed a persistent vascular supply to the acetabular labrum, even when macroscopic tears are present. This supply is provided by a vascular anastomotic ring surrounding the capsular attachment of the labrum, with limited contributions from the synovial lining or osseous acetabular rim²³. These findings were supported by Minokawa et al., who reported, in an in vivo study of patients with hip dysplasia, that laser Doppler flowmetry (LDF) showed that the blood flow in torn labrums was approximately equivalent to that

in normal labrums²⁴. LDF is a reproducible method for evaluating microvascular blood flow that has been used for >30 years in numerous clinical and research settings, including shoulder and knee arthroscopy²⁴⁻³⁶. However, to our knowledge, no study has directly assessed how variations in labral preservation affect blood flow¹.

Currently, most methods of labral augmentation and reconstruction employ the use of autografts or allografts that rely heavily on tissue metaplasia for ingrowth of a new blood supply, which may portend incomplete healing and integration of the graft tissue^{1,20,23,37-39}. In contrast, labral repair with concomitant capsular autograft augmentation is an established technique with favorable reported intermediate-term outcomes. Specifically, the use of local capsular autograft from the adjacent acetabular shelf has the theoretical advantage of salvaging the periacetabular blood supply by elevating and maintaining both the capsulolabral and chondrolabral tissue intact, as a single unit^{1,37-39}. Thus, the purpose of the present study was to assess the pattern of blood flow in patients with labral tears with use of LDF before and after arthroscopic labral repair with augmentation with capsular autograft. We hypothesized that this combined method of labral repair and augmentation would reduce, but not eliminate, blood flow to both the native labrum and the locally transferred capsular tissue.

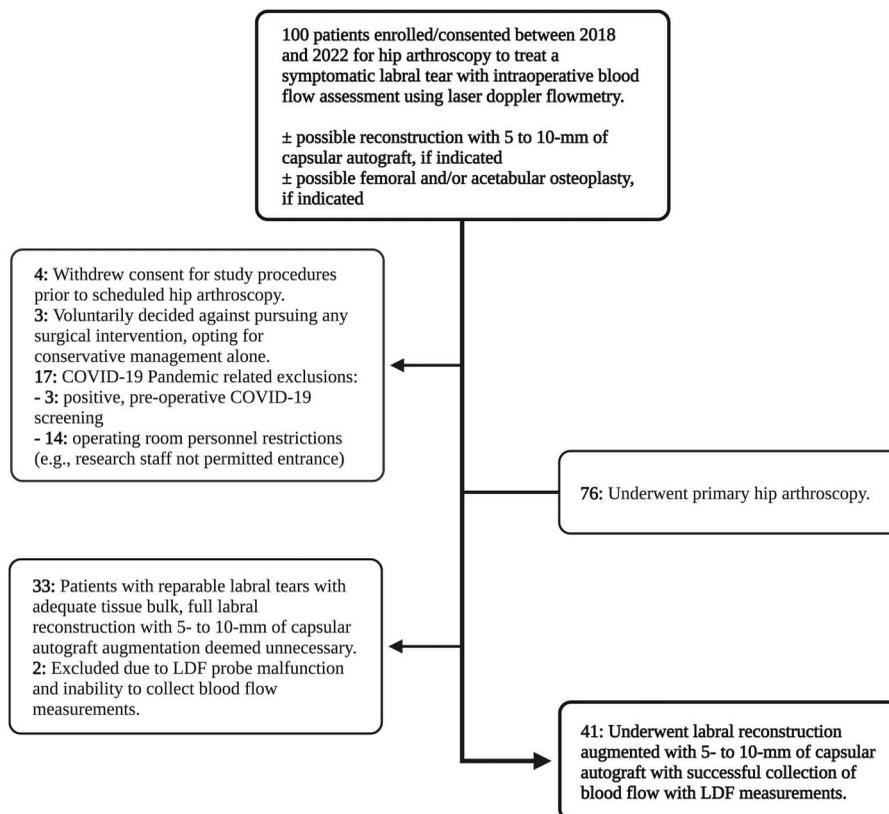


Fig. 1

Flow diagram detailing the inclusion of patients undergoing capsular autograft labral augmentation with laser Doppler flowmetry measurements.

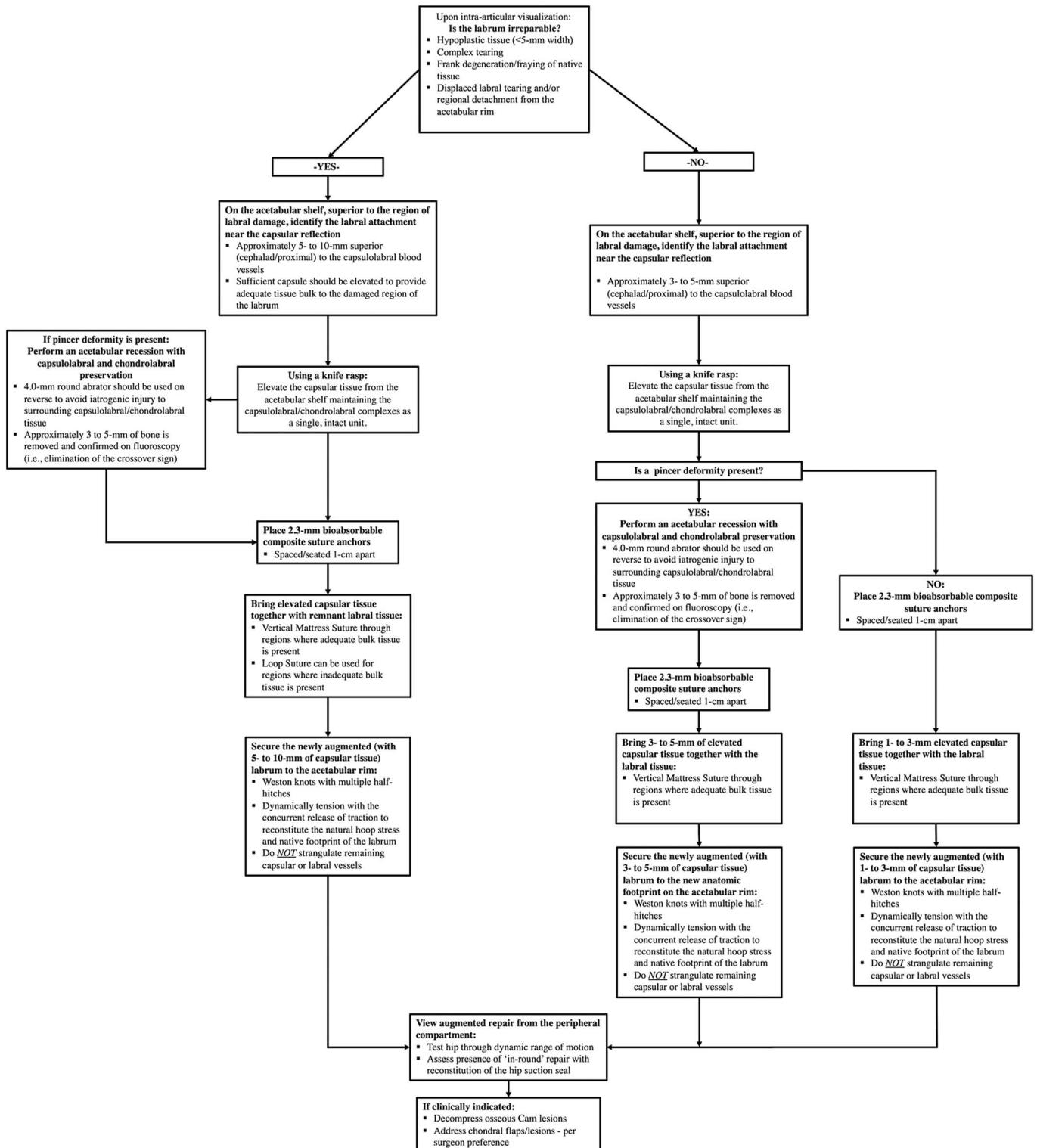


Fig. 2 Flow diagram detailing the clinical indications and applications of capsular augmentation during arthroscopic labral repair. (All patients included in the present study were found to have irreparable labral damage and were managed with an augmented repair with 5 to 10 mm of capsular autograft).

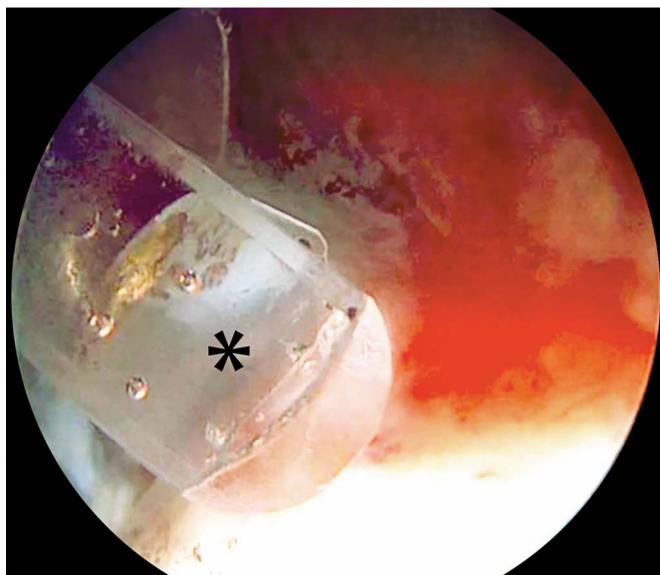


Fig. 3
Arthroscopic view showing the introduction of the laser Doppler flowmetry probe (asterisk; VP6a endoscopic probe) into the arthroscopic view.

Materials and Methods

Study Design

After institutional review board approval was obtained (Mass General Brigham #2017P002337), patients ≥ 18 years old were prospectively enrolled between 2018 and 2022. All patients had symptomatic acetabular labral tears and underwent arthroscopic labral repair with capsular augmentation; all procedures were performed by a single surgeon (S.D.M.) (Fig. 1). LDF measurements were performed for patients requiring 5 to 10 mm of capsular augment to reconstruct regions of severe, irreparable labral injury (Fig. 2)^{1,37,38}. The clinical indications for and applications of this technique are further discussed in the Appendix^{1,20,22,23,37-47}. All patients underwent similar preoperative evaluations that included clinical examination, appropriate imaging studies, diagnostic intra-articular anesthetic/corticosteroid injection, and a minimum of 3 months of nonoperative management, including formal physical therapy. Patients with persistent hip pain despite conservative interventions were offered hip arthroscopy. Patients were excluded if they had coagulopathy, if they had radiographic evidence of severe osteoarthritis (i.e., Tönnis grade ≥ 3), if they had had previous surgery on the affected hip, or if intraoperative LDF measurements could not be feasibly obtained^{1,37-39}.

Data Collection

Demographic and descriptive data, including age, sex, laterality, body mass index (BMI), lateral center-edge angle (LCEa), Tönnis angle, type of femoroacetabular impingement, and radiographic Tönnis classification, were collected. Intraoperative variables of interest included the Outerbridge classification of cartilage defects, the Beck classification of transition zone car-

tilage injury, concomitant arthroscopic procedures, the number of suture anchors, traction time, the method of suture tie-down, and the height of capsular elevation above the labral augmentation site. As previously described, labral tear size and location were documented for all patients with use of acetabular clock-face nomenclature⁴⁸. Last, anesthesia records were utilized to obtain arterial blood pressure readings that corresponded with the time of each flowmetry reading.

All measurements were collected intraoperatively with use of a fiber-optic, endoscopic probe (VP6a; 2.5-mW laser, 785-nm wavelength) of a laser Doppler vascular monitoring system (Moor Instruments) and were later analyzed with the company's moorVMS-PC software (version 4.1). In all cases, the 2.1-mm hemispherical tip of the LDF probe was introduced through a 5.5-mm cannula (Fig. 3) to measure blood flow within 1 mm³ of surrounding tissue as the blood cell flux (in perfusion units [PU])⁴⁹. Flux measurements are an arbitrary measure of perfusion, directly related to the product of the concentration and velocity of erythrocytes within the defined volume beneath the probe. More specifically, as the 2.5-mW laser light penetrates tissue, it is reflected by moving blood cells to produce a Doppler shift. The reflected light is then converted by the probe into electrical signals (blood cell flux) based on the frequency and magnitude of the Doppler shift. Flux is proportional to the blood flow and is the parameter most widely reported in the LDF literature^{26,28,29,50,51}.

The LDF probe was placed in direct contact with the tissue of interest, and continuous sampling at a rate of 40 Hz was recorded for each patient. To maintain a stable in vivo environment, all measurements were performed in a standardized manner by utilizing the least traction necessary to sample regions of interest, applying minimal force when contacting the probe tip to tissue, controlling for direct arthroscopic illumination to minimize flux signal interference, and arresting the arthroscopic pressure/flow pump to ensure physiological pressure within the joint. To reduce motion artifact and variations in contact pressure, measurements were performed "hands-free" by securing the probe to the mouth of the cannula.

Surgical Technique

All patients were positioned supine on a hip distraction table (Smith & Nephew). The hip arthroscopy technique used by the senior surgeon (S.D.M.) includes intra-articular fluid distension for initial portal placement, intermittent traction, sparing use of electrocautery, and acetabular recession with chondrolabral preservation^{39,47,52,53}. Additionally, to avoid transection of the iliofemoral ligament, puncture capsulotomy was carried out to facilitate intra-articular access^{54,55}.

Prior to addressing the labrum, the LDF probe was used to obtain measurements medial and lateral to the region of torn labral tissue (Fig. 4). An additional reading was obtained within the capsulolabral complex adjacent to the labral tear near its fibrocartilaginous capsular attachment (Fig. 5). Next, with use of a knife rasp, capsular tissue was elevated off the

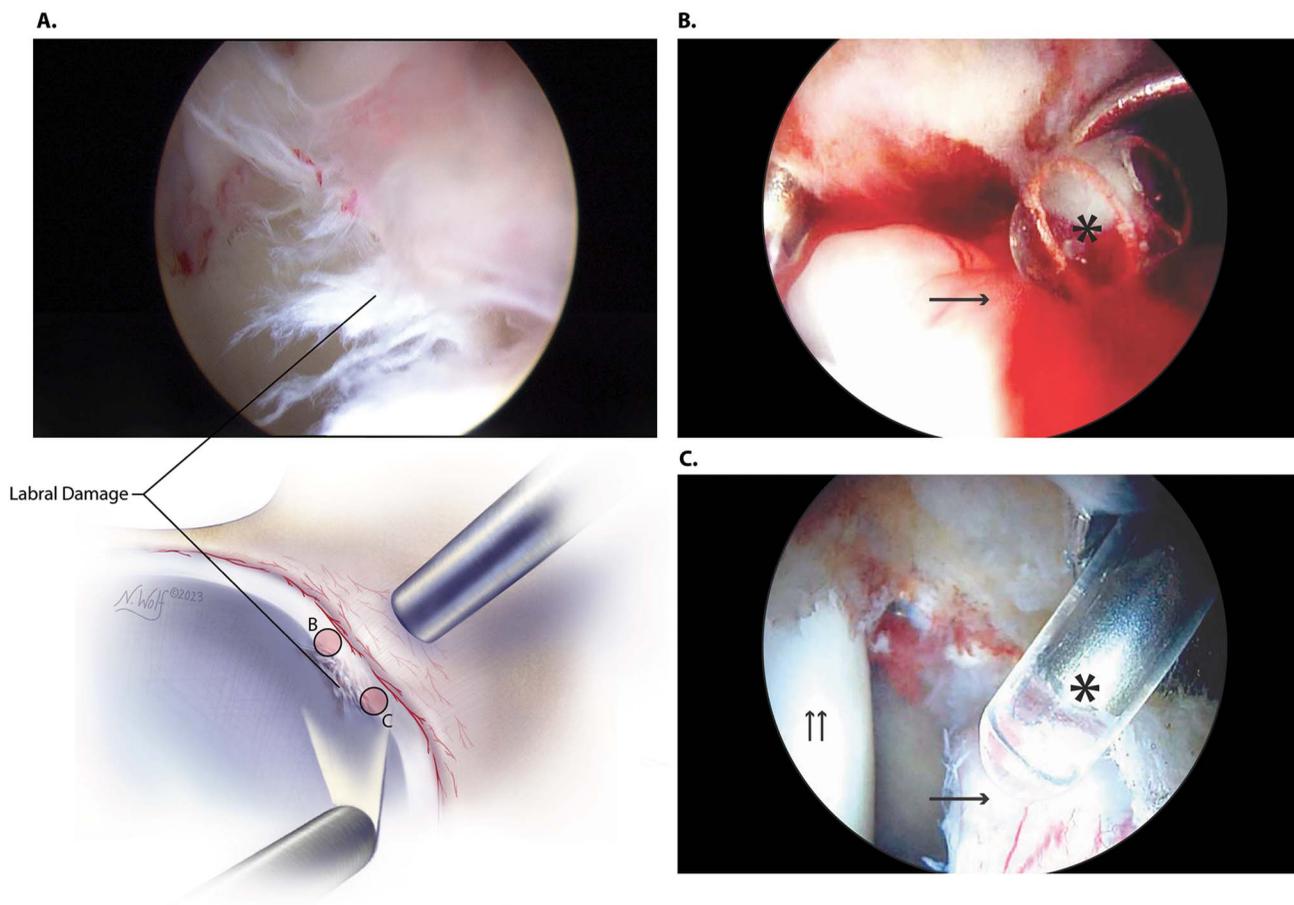


Fig. 4
Fig. 4-A Arthroscopic view of the right hip, showing the area of severe labral damage not amenable to repair with conventional methods. **Figs. 4-B and 4-C** Arthroscopic views showing placement of the LDF probe (*) on labral tissue (single arrows) medial (**Fig. 4-B**) and lateral (**Fig. 4-C**) to the region of damage. The double arrows indicate the femoral head. In the corresponding illustration (bottom left panel), the red circles indicate the regions where the LDF probe was placed for measurements. (Illustration by Nicole Wolf, MS ©2023.)

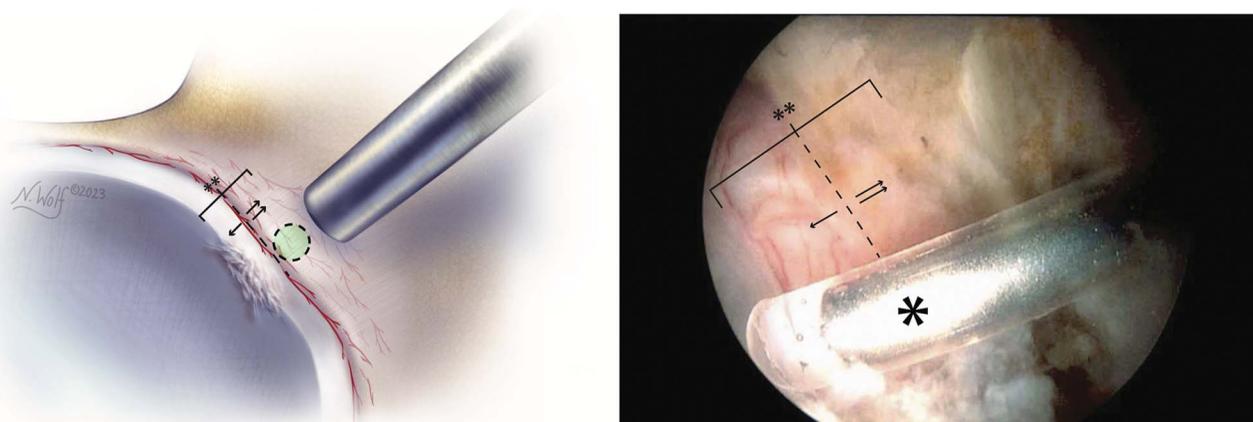


Fig. 5
 The right panel shows an arthroscopic view of the LDF probe (single asterisk) at the capsulolabral complex (double asterisk with bracket and dashed line) with adjacent capsule (double arrows) and capsulolabral vessels (single arrow). LDF measurements were performed within the region of the capsulolabral complex superior to the region of labral damage before elevation of the capsular tissue. In the corresponding illustration (left panel), the green circle indicates the region where the LDF probe was placed within the region of the capsulolabral complex. (Illustration by Nicole Wolf, MS ©2023.)

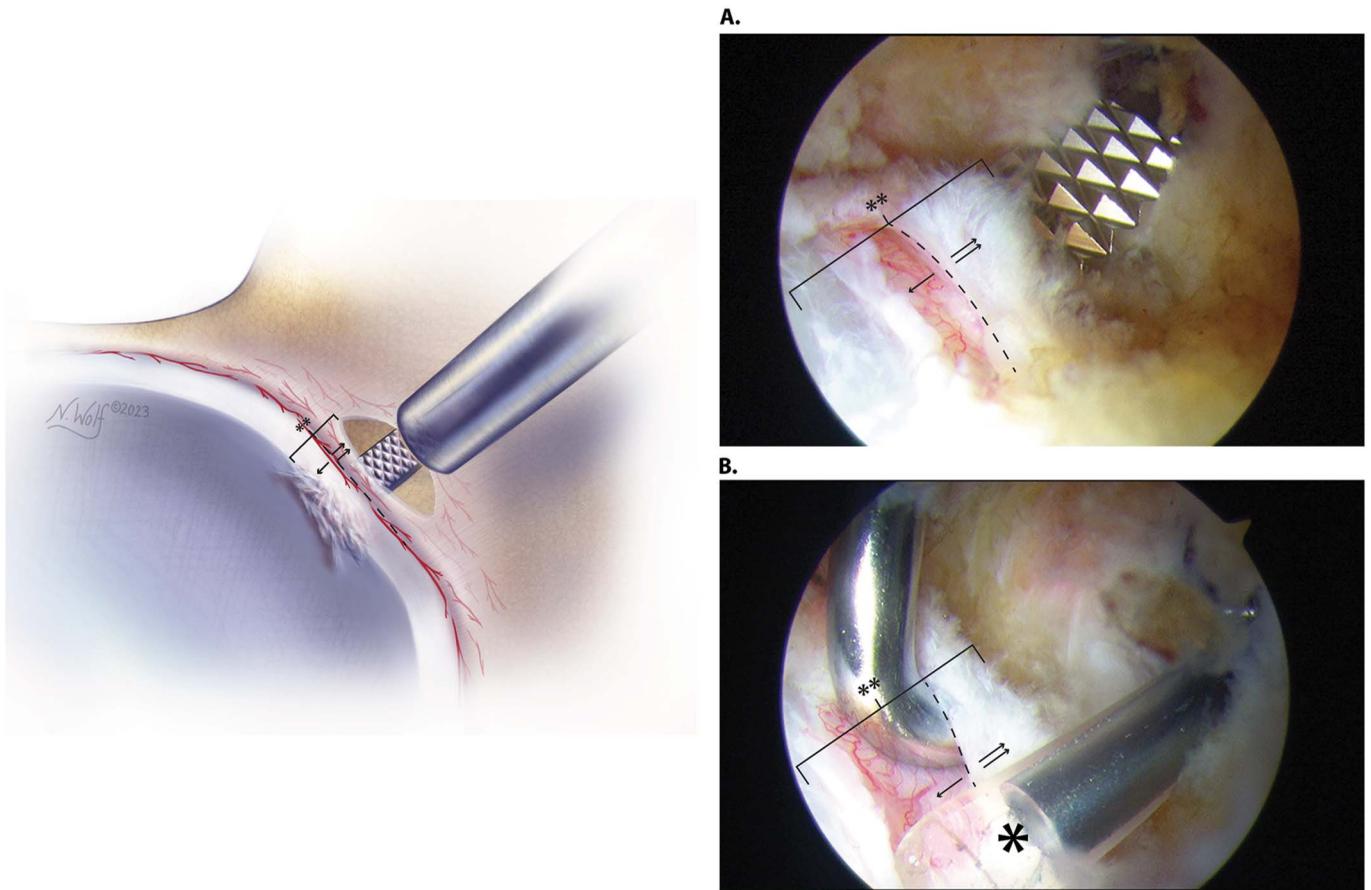


Fig. 6

Figs. 6-A Arthroscopic view (and corresponding illustration) showing knife rasp elevation of the adjacent capsule (double arrows) superior to the capsulolabral complex (double asterisk with bracket and dashed line) above the region of labral damage. Note the transition of the capsulolabral vessels into the labrum (single arrow). **Fig. 6-B** Following knife rasp elevation, arthroscopic view of the LDF probe (single asterisk) placement at the capsulolabral complex (double asterisk with bracket and dashed line) with adjacent capsule (double arrows) and transition of the capsulolabral vessels into the labrum (single arrow). (Illustration by Nicole Wolf, MS ©2023.)

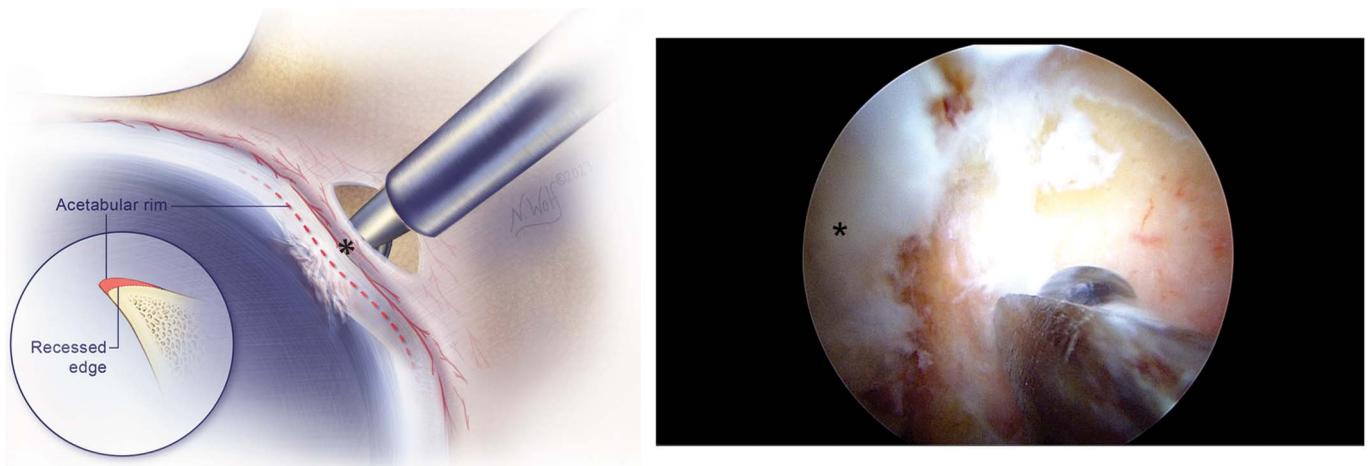


Fig. 7

The right panel shows an arthroscopic view of a hip with concomitant pincer-type impingement. In such cases, the underlying acetabular shelf was contoured, under fluoroscopic guidance, with use of a 4.0-mm round abradar on reverse. It is important to use the abradar on reverse to avoid damaging the elevated capsulolabral tissue/vessels (single asterisk) and adjacent chondrolabral junction. In the corresponding illustration (left panel), the dashed red line denotes the contour of the pincer lesion underlying the capsulolabral complex. (Illustration by Nicole Wolf, MS ©2023.)

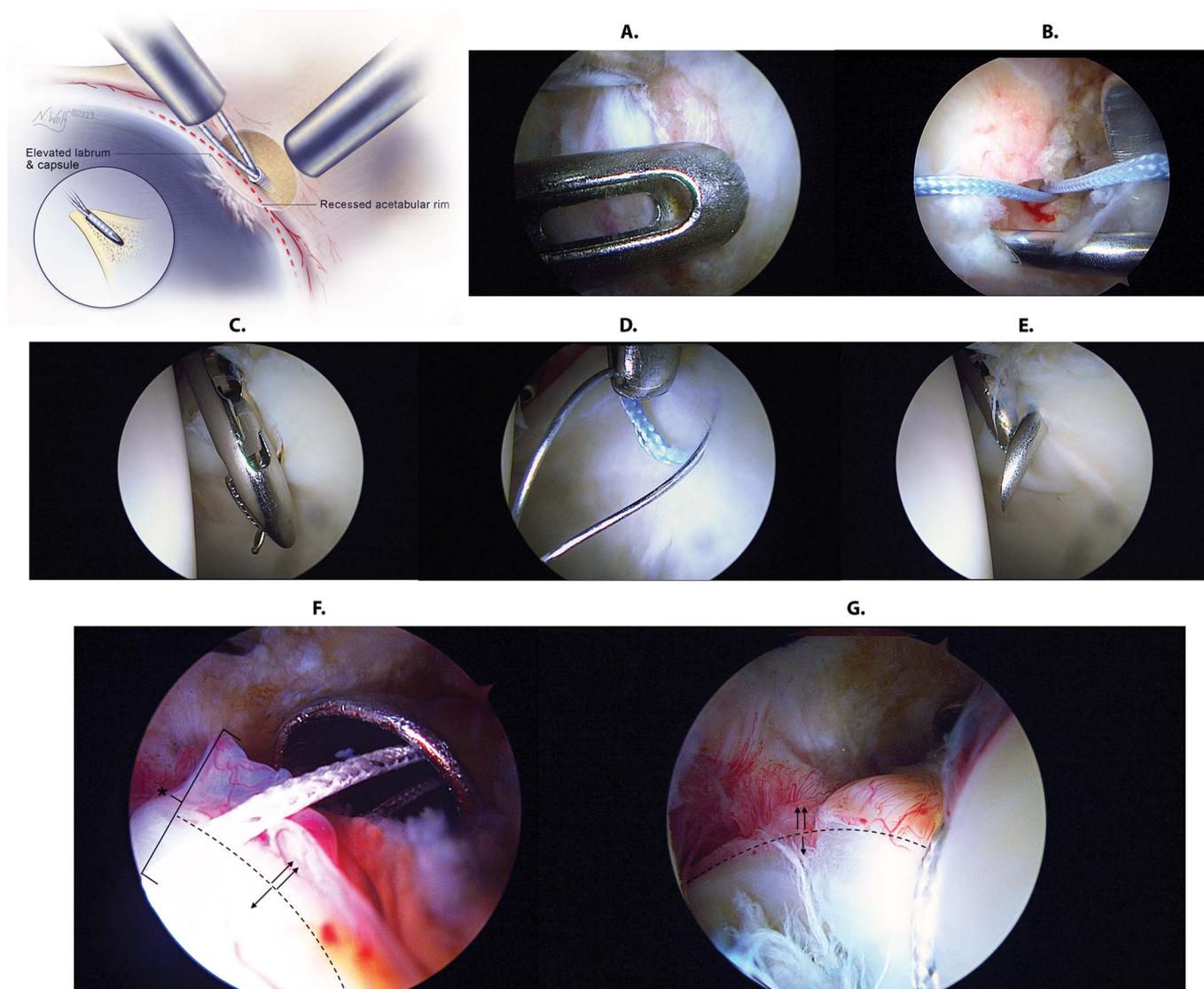


Fig. 8
Figs. 8-A through 8-G Following the seating of a 2.3-mm bioabsorbable anchor into the recessed acetabular rim (**Figs. 8-A and 8-B**), suture is shuttled (**Figs. 8-C, 8-D, and 8-E**) in a loop fashion (**Figs. 8-F and 8-G**). The suture brings together the elevated capsular tissue (double arrows) and the remaining labral tissue (single arrow). In Figure 8-F, the asterisk denotes the construct combining labral tissue with capsular autograft. In the corresponding illustration, the dashed red line denotes the newly recontoured acetabular rim. (Illustration by Nicole Wolf, MS ©2023.)

acetabular shelf, with gentle maneuvering to preserve the capsulolabral blood supply, approximately 5 to 10 mm above the region of the labrum to be augmented (Fig. 6-A). For concomitant acetabular recession, knife rasp elevation was continued in order to visualize the underlying pincer lesion while strictly maintaining the capsulolabral/chondrolabral complexes as a single, continuous unit. The underlying shelf was then contoured, under fluoroscopic guidance, with use of a 4.0-mm round abradar on reverse (Fig. 7)^{1,39}. Immediately following capsular elevation and possible acetabuloplasty, the LDF probe was reintroduced into the hip joint under direct arthroscopic visualization to obtain another

measurement of the same segment of capsular tissue within the capsulolabral complex (Fig. 6-B).

This same region of elevated capsular tissue was then brought together with the remaining labral tissue and was seated to the acetabular rim with use of 2.3-mm bioabsorbable composite suture anchors (Fig. 8). To ensure an “in-round” repair, Weston knots with multiple half-hitches were dynamically tensioned with the concurrent release of traction^{37,47}. Most repairs required the use of loop sutures, but the vertical mattress technique was employed if adequate tissue bulk was available. All anchors were seated approximately 1 cm apart, with knots tied posterior to the augmented capsular tissue to

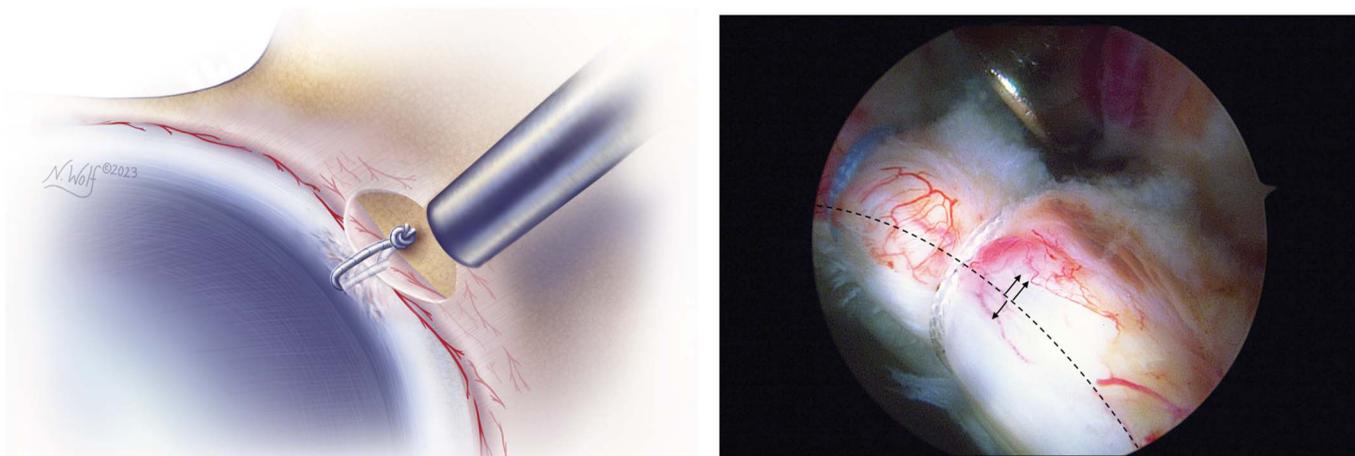


Fig. 9
The right panel shows an arthroscopic view from the anterolateral portal, displaying the final construct combining labral tissue (single arrow) with capsular autograft (double arrow). The dashed line grossly delineates the capsulolabral transition zone within the new reconstructed labrum. The corresponding illustration (left panel) shows the position of knot tie-down, posterior to the augmented capsular tissue. (Illustration by Nicole Wolf, MS ©2023.)

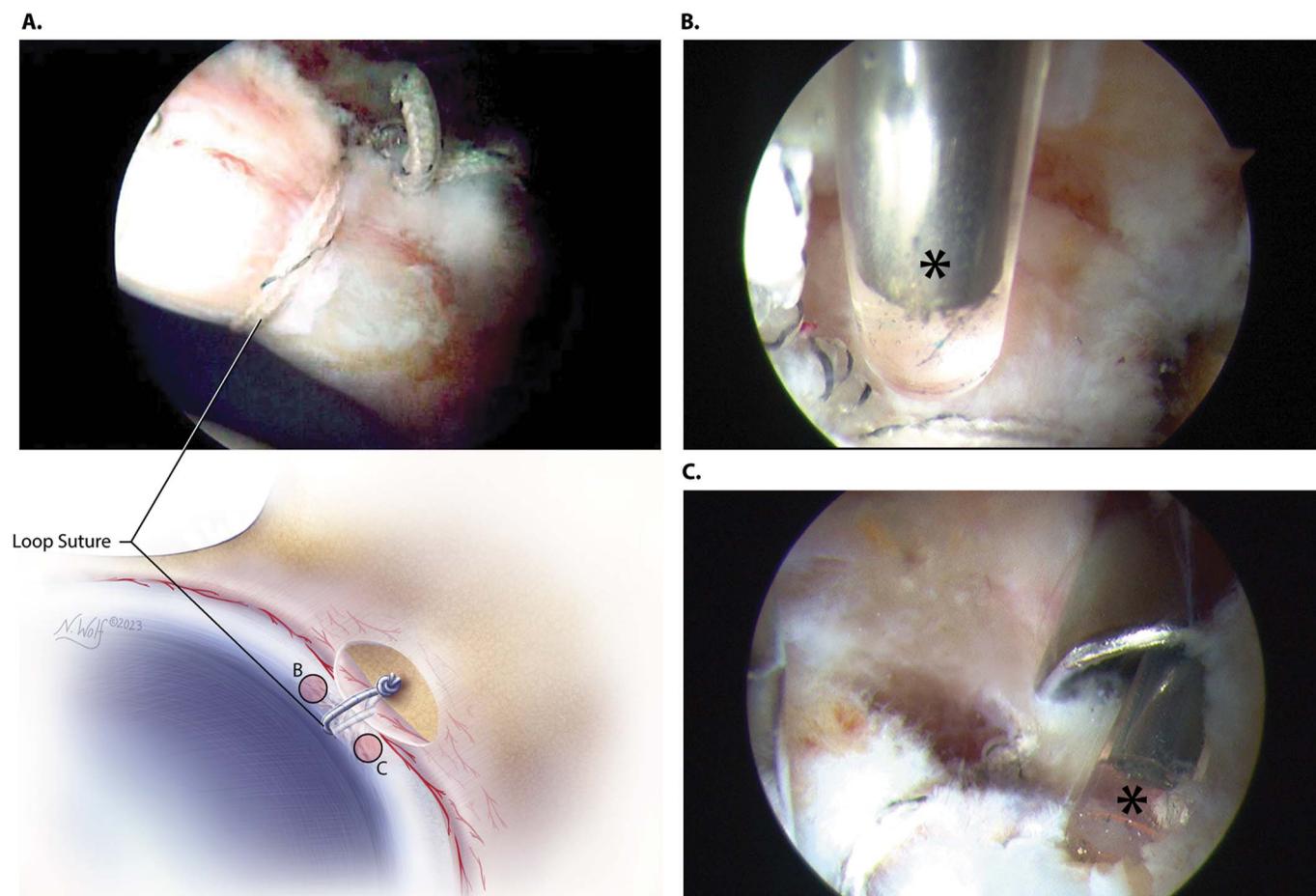


Fig. 10
Fig. 10-A Arthroscopic view showing the final labral construct, with placement of the arthroscopic knot posterior to the augmented capsular tissue.
Figs. 10-B and 10-C Arthroscopic views made during the final LDF probe readings of labral tissue medial (**Fig. 10-B**) and lateral (**Fig. 10-C**) to the region of the tear. The asterisk indicates the probe. In the corresponding illustration (bottom left panel), the red circles indicate regions where the LDF probe was placed for final measurements following suture tie-down. (Illustration by Nicole Wolf, MS ©2023.)

TABLE I Baseline Demographic Characteristics (N = 41) *

Age* (yr)	31.3 ± 8.4
Age group (no. of patients)	
18-30 yr	22 (53.7%)
>30 yr	19 (46.3%)
Body mass index* (kg/m ²)	24.6 ± 3.4
Body mass index category (no. of patients)	
Normal (≤24.9 kg/m ²)	23 (56.1%)
Overweight (25-29.9 kg/m ²)	14 (34.1%)
Obese (≥30 kg/m ²)	4 (9.8%)
Sex (no. of patients)	
Female	17 (41.5%)
Male	24 (58.5%)
Laterality (no. of patients)	
Left	14 (34.1%)
Right	27 (65.9%)
ASA classification† (no. of patients)	
1	20 (48.8%)
2	21 (51.2%)
Radiographic findings* (deg)	
Lateral center-edge angle	35.3 ± 4.9
Tönnis angle	5.8 ± 5.8
Alpha angle	69.1 ± 9.89
Mean arterial pressure* (mm Hg)	93.7 ± 10.9
Type of femoroacetabular impingement (no. of patients)	
Cam	3 (7.3%)
Pincer	21 (51.2%)
Mixed cam and pincer	17 (41.5%)
Tönnis classification (no. of patients)	
Grade 0	22 (53.7%)
Grade 1	17 (41.5%)
Grade 2	2 (4.9%)
Grade 3	0 (0%)

*The values are given as the mean and the standard deviation.
†ASA = American Society of Anesthesiologists.

avoid vessel strangulation (Fig. 9)⁵⁶. After tensioning, seating, and tie-down, reconstitution of the labral seal was confirmed during dynamic examination from the peripheral compartment. The LDF probe was then inserted for the last time to obtain final medial and lateral measurements within the new, augmented labral construct surrounding the area of the tear (Fig. 10).

Statistical Analysis

The laser Doppler vascular monitoring system has a reported accuracy of ±10% and precision of ±3% (per Moor Instruments). As such, an a priori power analysis revealed

that 17 patients would be needed to yield 80% power to detect a 10% between-subject difference in flux measurements (i.e., medial versus lateral perfusion), whereas 10 patients would be needed to detect within-subject differences (i.e., perfusion before versus after capsular elevation).

TABLE II Intraoperative Variables (N = 41)

Tear size* (deg)	79.8 ± 19.2
Localization of tears† (no. of patients)	
Posterior (<10:00)	18 (43.9%)
Posterosuperior (10:00-12:00)	20 (48.8%)
Anterosuperior (12:00-2:00)	22 (53.7%)
Anterior (>2:00)	19 (46.3%)
Traction time* (min)	71.8 ± 5.9
Outerbridge classification (no. of patients)	
Grade 1	3 (7.3%)
Grade 2	10 (24.4%)
Grade 3	22 (53.7%)
Grade 4	6 (14.6%)
Beck classification of transition zone cartilage injury (no. of patients)	
Stage 0	1 (2.4%)
Stage 1	14 (34.1%)
Stage 2	17 (41.5%)
Stage 3	9 (22.0%)
Stage 4	0 (0%)
Osteoplasty procedure performed (no. of patients)	
Acetabuloplasty only	19 (46.3%)
Femoroplasty only	4 (9.8%)
Femoroacetabuloplasty	18 (43.9%)
Amount of capsule used for labral augmentation	
Mean* (mm)	7.5 ± 2.8
≤7 mm (no. of patients)	22 (53.7%)
>7 mm (no. of patients)	19 (46.3%)
Chondral flap (no. of patients)	
No	31 (75.6%)
Yes	10 (24.4%)
Suture anchors used (no. of patients)	
1	1 (2.4%)
2	12 (29.3%)
3	28 (68.3%)
Suture technique (no. of patients)	
Loop	34 (82.9%)
Vertical mattress	7 (17.1%)

*The values are given as the mean and the standard deviation.
†Relative to standard clock-face nomenclature. Note that some tears extended into multiple regions and therefore the percentages do not add up to 100%³⁴.

TABLE III Labral Tissue Microvascular Blood Flow Flux Measured with Use of LDF

	Flux Measurement*† (PU)	No. of LDF Measurements*	Percent Change in Flux Measurements‡
Before labral reconstruction			
Medial to region of tear	107.0 ± 25.7	798.3 ± 365.1	—
Lateral to region of tear	134.5 ± 44.5	849.1 ± 369.6	—
After labral reconstruction			
Medial to region of tear	81.3 ± 20.2	689.8 ± 339.2	−22.3 (−32.7, −11.9)
Lateral to region of tear	84.4 ± 21.9	679.1 ± 382.4	−32.5 (−41.5, −23.6)
Before capsular elevation			
Labral tissue adjacent to capsular attachment	115.3 ± 22.3	391.7 ± 264.1	—
After capsular elevation			
Labral tissue adjacent to capsular attachment	99.8 ± 19.7	496.2 ± 498.9	−9.24 (−18.1, −0.04)

*The values are given as the mean and the standard deviation. †PU = perfusion units. ‡The values are given as the percent change, with the 95% CI in parentheses.

Mean baseline measurements of flux at each location were compared with corresponding readings following capsular elevation and after completing labral augmentation (both medial and lateral to the region of the tear). Specific to each patient, flux changes were calculated and expressed as the percent change from the mean baseline measurement at each location. Statistical analysis was performed with use of SPSS Statistical Software (version 27; IBM). Categorical variables were analyzed with use of the chi-square test or the Fisher exact test, as appropriate. The percent change in blood flow flux was analyzed with use of either the Student *t* test or 1-way analysis of variance (ANOVA) using the Tukey method if multiple comparisons were made. Associations between preoperative demographic characteristics and labral perfusion were analyzed with use of linear regression analyses. All reported *p* values were 2-tailed, with the level of significance set at $\alpha = 0.05$.

Source of Funding

This study was supported by the Conine Family Fund for Joint Preservation.

Results

LDF measurements were obtained and analyzed for 41 of the 100 patients who were enrolled in the study. This cohort included 24 men (58.5%) and 17 women (41.5%) with a mean age (and standard deviation [SD]) of 31.3 ± 8.4 years, a mean BMI of 24.6 ± 3.4 kg/m², a mean LCEa of $35.3^\circ \pm 4.9^\circ$, a mean Tönnis angle of $5.8^\circ \pm 5.8^\circ$, a mean alpha angle of $69.1^\circ \pm 9.9$, and a mean arterial pressure of 93.7 ± 10.9 mm Hg. In terms of radiographic osteoarthritis, 53.7%, 41.5%, and 4.9% of hips had Tönnis grades of 0, 1, and 2, respectively (Table I). The mean tear size was $79.8^\circ \pm 19.2^\circ$, and the mean height of capsular reflection above the region of labral augmentation was 7.5 ± 2.8 mm. Additionally, 37 patients (90.2%) underwent acetabuloplasty and 22 (53.7%)

underwent femoroplasty. All patients received segmental augmentation with loop suture repair (34 patients; 82.9%) or vertical mattress repair (7 patients; 17.1%). Data on the Outerbridge classification of cartilage defects, the Beck classification of transition zone cartilage injury, and the presence of a chondral flap are reported in Table II.

The initial blood flow output signal was pulsatile both medial and lateral to the region of the tear and superior to the tear near the capsular attachment of the labrum. Continuous LDF sampling collected a total of 163,658 flux measurements, with a mean of 665.3 ± 432.7 samples per location. Following capsular elevation, the mean percent change in blood flow flux was significantly different from baseline (−9.24% [95% confidence interval (CI), −18.1% to −0.04%]; $p < 0.001$). Following labral augmentation, the percent change in blood flow flux decreased significantly both medially (−22.3% [95% CI, −32.7% to −11.9%]; $p < 0.001$) and laterally (−32.5% [95% CI, −41.5% to −23.6%]; $p = 0.041$) (Table III). There was no significant difference between the changes in medial and lateral flux measurements following repair (mean difference, −10.2% [95% CI, −23.8% to 3.3%]; $p = 0.136$). Unadjusted analyses stratifying for age, BMI, sex, type of impingement, osteoarthritis severity (e.g., Tönnis/Outerbridge class), arthroscopic procedure performed, amount of capsule used for augmentation, presence of a chondral flap, number of anchors used, tear size, traction time, and suture technique revealed that none of these factors were associated with significant differences in labral blood flow flux medially or laterally ($p > 0.05$ for all) (Table IV). Finally, multiple regression analyses examining the effects of demographic and intraoperative variables on blood flow demonstrated that age, BMI, suture technique, and amount of capsule used for augmentation were not significantly associated with changes in medial or lateral flux measurements following repair augmentation with capsular autograft ($p > 0.05$ for all) (Table V).

TABLE IV Mean Percent Change in Microvascular Blood Flow Flux Following Labral Augmentation with Capsular Autograft*

	Lateral (%)	P Value	Medial (%)	P Value
Age		0.82		0.20
18-30 yr	-31.6 (-44.4, -18.8)		-28.6 (-42.2, -15.0)	
>30 yr	-33.6 (-47.4, -19.8)		-15.3 (-32.0, 1.5)	
Body mass index		0.35		0.34
Normal (≤ 24.9 kg/m ²)	-35.4 (-47.6, -23.2)		-27.8 (-42.0, -13.6)	
Overweight (25-29.9 kg/m ²)	-22.1 (-40.3, -3.9)		-11.4 (-31.4, 8.6)	
Obese (≤ 30 kg/m ²)	-37.3 (-60.7, -14.0)		-25.3 (-67.6, 17.0)	
Sex		0.95		0.42
Female	-32.2 (-46.9, -17.5)		-27.1 (-44.4, -9.9)	
Male	-32.7 (-43.6, -21.9)		-18.7 (-30.9, -6.4)	
Type of femoroacetabular impingement		0.52		0.94
Isolated cam	-39.5 (-148.7, 69.7)		-28.4 (-113.7, 56.9)	
Isolated pincer	-27.5 (-41.3, -13.8)		-21.3 (-38.9, -3.7)	
Combined	-37.5 (-49.7, -25.2)		-22.4 (-35.5, -9.3)	
Tönnis classification		0.35		0.70
Grade 0	-30.1 (-39.1, -21.0)		-20.1 (-31.4, -8.7)	
Grade 1	-32.3 (-51.0, -13.7)		-26.6 (-47.9, -5.3)	
Grade 2	-60.8 (-309.4, 187.9)		-8.9 (-258.2, 240.4)	
Outerbridge classification		0.83		0.13
Grade 1 or 2	-31.1 (-42.0, -20.2)		-33.7 (-46.7, -20.7)	
Grade 3 or 4	-33.2 (-45.0, -21.4)		-16.8 (-30.0, -3.5)	
Procedure performed		0.27		0.81
Labral repair and acetabuloplasty	-24.8 (-38.9, -10.8)		-21.0 (-39.3, -2.7)	
Labral repair and femoral neck osteoplasty	-36.1 (-94.8, 22.5)		-14.4 (-67.6, 38.8)	
Labral repair and femoroacetabuloplasty	-39.8 (-52.3, -27.3)		-25.6 (-39.5, -11.6)	
Amount of capsule used for labral augmentation, mm (<i>correlation</i>)	-0.11 (-0.41, 0.20)	0.48	0.22 (-0.10, 0.50)	0.17
Chondral flap		0.80		0.27
No	-33.2 (-44.0, -22.4)		-19.2 (-31.7, -6.7)	
Yes	-30.5 (-43.6, -17.4)		-33.0 (-44.3, -21.6)	
Suture anchors used		0.78		0.20
1-2	-34.6 (-55.2, -14.0)		-32.4 (-53.2, -11.5)	
3	-31.6 (-41.6, -21.5)		-17.4 (-29.7, -5.1)	
Tear size, deg (<i>correlation</i>)	-0.11 (-0.40, 0.20)	0.49	0.17 (-0.15, 0.45)	0.45
Traction time, min (<i>correlation</i>)	-0.08 (-0.38, 0.23)	0.23	0.04 (-0.28, 0.34)	0.34
Suture technique		0.61		0.16
Loop	-33.6 (-43.2, -23.9)		-18.9 (-30.2, -7.6)	
Vertical mattress	-27.4 (-48.1, -6.7)		-38.2 (-57.9, -18.5)	

*The values are reported as the mean percent change or the correlation coefficient, with the 95% CI in parentheses.

Discussion

Following the initial association between labral lesions and accelerated rates of chondral degeneration, hip arthroscopy utilization and related research have dramatically increased^{16,57-59}. However, to our knowledge, no investigations have evaluated labral blood flow in vivo following arthroscopic repair of labral

tears. The use of LDF in clinical research has been validated in numerous clinical settings and has been shown to provide robust data on the microcirculation in a variety of tissues^{24-31,60}. The present study evaluated blood flow with use of LDF in regions of the labrum and capsular tissue during acetabular labral repair with capsular autograft augmentation. The results of this study

TABLE V Multiple Regression Analysis Evaluating Effects of Patient Characteristics and Suture Placement on Percent Change in Labral Microvascular Blood Flow Flux

	Lateral		Medial	
	Unstandardized Coefficient (95% CI)	P Value	Unstandardized Coefficient (95% CI)	P Value
Age (% change per yr)	0.2 (−0.9, 1.4)	0.67	0.5 (−0.7, 1.8)	0.39
Body mass index (% change per kg/m ²)	1.0 (−1.9, 3.9)	0.49	1.1 (−2.2, 4.3)	0.51
Vertical mattress suture technique* (% change)	9.7 (−16.0, 35.3)	0.45	−15.4 (−44.2, 13.4)	0.28
Amount of capsule used for labral augmentation (% change per mm)	−1.2 (−5.5, 3.1)	0.58	1.3 (−3.6, 6.1)	0.60

*Reference: Loop suture technique.

support our hypothesis that this method of repair with augmentation reduced, but did not eliminate, blood flow to both the native labrum and the locally transferred capsular tissue. On average, a 9.24% reduction in LDF flow values was observed when evaluating perfusion to the capsulolabral complex after elevating capsular tissue for local transfer. Additionally, a decrease in blood flow flux of 22.3% medially and 32.5% laterally was noted in labral tissue surrounding the tear following final suture tie-down. While maintaining the native blood supply may not be emphasized in other variations of hip-preservation surgery, these findings provide evidence that blood flow to the labrum is indeed present, measurable, and susceptible to change with surgical manipulation.

Furthermore, given that all labral flux measurements were initially pulsatile, our findings support existing literature that labral tissue maintains some degree of perfusion even in the setting of concomitant tears^{23,24}. Additionally, changes in labral blood flow flux were not found to be significantly different on the basis of Tönnis/Outerbridge grades or the presence of a chondral flap, suggesting that chondral injury severity was not predictive of blood flow changes to the labrum and/or capsule. This finding aligns with cadaveric assessments of circulation to the native labrum, as Kelly et al. reported that labral blood flow was heavily skewed to the capsular half, with limited contributions stemming from the chondrolabral junction and adjacent articular cartilage⁴⁰. Translational studies have highlighted the benefit of arthroscopic repair in the ovine model by displaying the healing potential of the labrum via fibrovascular scarring⁶¹. Although it remains unclear what degree of healing can be achieved in humans, maintaining blood flow to the labrum and augmented tissue likely would provide the optimum environment to maximize healing, sustain tissue viability, and ensure sustained reconstitution of the hip suction seal^{20,23}. Our results lend further credence to the use of labrum-preserving techniques that aim to both reconstitute the native hip anatomy and prioritize sparing the remaining blood supply when possible.

While this is the first study to utilize LDF to investigate blood flow in the setting of hip-preservation surgery, we

acknowledge that it is not without limitations. First, although LDF has been validated to provide robust data on microcirculation in vivo, there may have been secondary operative factors that could not be controlled^{24-31,60}. However, appropriate precautions were taken by standardizing our measurement technique, employing continuous sampling to reduce variability, and mitigating confounding variables by normalizing variations in flux on a case-by-case basis (i.e., calculating percent change at the patient level). Second, blood flow measurements are cross-sectional assessments and may change over time. As such, in relation to the presented technique, the reported changes in flux may only apply to the initial time point of fixation and the clinical relevance will require correlation with future investigations. Third, given that there are no other studies evaluating labral blood flow in vivo concerning alternative repair methods, no definitive control exists to extrapolate the minimum perfusion threshold required to sustain tissue viability. Thus, the future ability to differentiate functional from merely measurable flow is of critical interest, and the consistent, tight grouping of our absolute flux readings may suggest that the biological range of flow values within the acetabular labrum may be narrow³⁵. Additionally, given conflicting evidence regarding the optimum number of subjects per predictor parameter, it is possible that our multiple regression analysis was susceptible to a type-II error^{62,63}. Overall, we established that a change in blood flow does indeed exist; thus, determining clinically important thresholds for baseline labral perfusion, tensioning of repair sites, and correlation of flow rates with healing and successful clinical outcomes represent exciting areas of future investigation²⁶.

Conclusions

Labral repair with capsular augmentation sustains a reduced blood flow to the native labrum and capsular tissue at the time of fixation. The biological importance of this reduction is unknown, but these findings may serve as a benchmark for other labral preservation techniques and support future correlations with clinical outcomes.

Appendix

 Supporting material provided by the authors is posted with the online version of this article as a data supplement at [jbjs.org \(http://links.lww.com/JBJSOA/A557\)](http://links.lww.com/JBJSOA/A557). ■

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References

- Nwachukwu BU, McCormick F, Martin SD. Arthroscopic technique for chondrolabral capsular preservation during labral repair and acetabular osteoplasty. *Arthrosc Tech*. 2013 Jun 14;2(3):e213-6.
- Ferguson SJ, Bryant JT, Ganz R, Ito K. The acetabular labrum seal: a poroelastic finite element model. *Clin Biomech (Bristol, Avon)*. 2000 Jul;15(6):463-8.
- Ferguson SJ, Bryant JT, Ganz R, Ito K. An in vitro investigation of the acetabular labral seal in hip joint mechanics. *J Biomech*. 2003 Feb;36(2):171-8.
- Ferguson SJ, Bryant JT, Ganz R, Ito K. The influence of the acetabular labrum on hip joint cartilage consolidation: a poroelastic finite element model. *J Biomech*. 2000 Aug;33(8):953-60.
- Cadet ER, Chan AK, Vorys GC, Gardner T, Yin B. Investigation of the preservation of the fluid seal effect in the repaired, partially resected, and reconstructed acetabular labrum in a cadaveric hip model. *Am J Sports Med*. 2012 Oct;40(10):2218-23.
- McCarthy JC, Noble PC, Schuck MR, Wright J, Lee J. The Otto E. Aufranc Award: The role of labral lesions to development of early degenerative hip disease. *Clin Orthop Relat Res*. 2001 Dec;(393):25-37.
- Kucharik MP, Abraham PF, Nazal MR, Varady NH, Eberlin CT, Meek WM, Martin SD. Arthroscopic Acetabular Labral Repair Versus Labral Debridement: Long-term Survivorship and Functional Outcomes. *Orthop J Sports Med*. 2022 Jul 7;10(7):23259671221109012.
- Krych AJ, Thompson M, Knutson Z, Scoon J, Coleman SH. Arthroscopic labral repair versus selective labral debridement in female patients with femoroacetabular impingement: a prospective randomized study. *Arthroscopy*. 2013 Jan;29(1):46-53.
- Larson CM, Giveans MR. Arthroscopic debridement versus refixation of the acetabular labrum associated with femoroacetabular impingement. *Arthroscopy*. 2009 Apr;25(4):369-76.
- Larson CM, Giveans MR, Stone RM. Arthroscopic debridement versus refixation of the acetabular labrum associated with femoroacetabular impingement: mean 3.5-year follow-up. *Am J Sports Med*. 2012 May;40(5):1015-21.
- Larson CM, Dean RS, McGaver RS, Seiffert KJ, Giveans MR. Arthroscopic Debridement Versus Refixation of the Acetabular Labrum Associated With Femoroacetabular Impingement: Updated Mean 7-Year Follow-up. *Am J Sports Med*. 2022 Mar;50(3):731-8.
- Philippon MJ, Bolia IK, Locks R, Briggs KK. Labral Preservation: Outcomes Following Labrum Augmentation Versus Labrum Reconstruction. *Arthroscopy*. 2018 Sep;34(9):2604-11.
- Amar E, Sampson TG, Sharfman ZT, Caplan A, Rippe N, Atzman R, Drexler M, Rath E. Acetabular labral reconstruction using the indirect head of the rectus femoris tendon significantly improves patient reported outcomes. *Knee Surg Sports Traumatol Arthrosc*. 2018 Aug;26(8):2512-8.
- Carreira DS, Kruchten MC, Emmons BR, Martin RL. Arthroscopic labral reconstruction using fascia lata allograft: shuttle technique and minimum two-year results. *J Hip Preserv Surg*. 2018 Aug 10;5(3):247-58.
- Redmond JM, Cregar WM, Martin TJ, Vemula SP, Gupta A, Domb BG. Arthroscopic Labral Reconstruction of the Hip Using Semitendinosus Allograft. *Arthrosc Tech*. 2015 Jul 27;4(4):e323-9.
- Matsuda DK, Burchette RJ. Arthroscopic hip labral reconstruction with a gracilis autograft versus labral refixation: 2-year minimum outcomes. *Am J Sports Med*. 2013 May;41(5):980-7.
- Rathi R, Mazek J. Arthroscopic Acetabular Labral Reconstruction with Fascia Lata Allograft: Clinical Outcomes at Minimum One-Year Follow-Up. *Open Orthop J*. 2017 Jul 25;11:554-61.
- Deshmane PP, Kahlenberg CA, Patel RM, Han B, Terry MA. All-arthroscopic iliotibial band autograft harvesting and labral reconstruction technique. *Arthrosc Tech*. 2012 Dec 17;2(1):e15-9.
- Geyer MR, Philippon MJ, Fagreluis TS, Briggs KK. Acetabular labral reconstruction with an iliotibial band autograft: outcome and survivorship analysis at minimum 3-year follow-up. *Am J Sports Med*. 2013 Aug;41(8):1750-6.
- Su T, Ao Y, Yang L, Chen GX. The Vascularization Course of Labral Autograft and Its Effect on Tissue Healing: Acetabular Labral Augmentation Versus Labral Reconstruction in a Porcine Model. *Am J Sports Med*. 2022 Aug;50(10):2647-58.
- Shi YY, Chen LX, Xu Y, Hu XQ, Ao YF, Wang JQ. Acetabular Labral Reconstruction With Autologous Tendon Tissue in a Porcine Model: In Vivo Histological Assessment and Gene Expression Analysis of the Healing Tissue. *Am J Sports Med*. 2016 Apr;44(4):1031-9.
- Suppauksorn S, Parvaresh KC, Rasio J, Shewman EF, Nho SJ. The Effect of Rim Preparation, Labral Augmentation, and Labral Reconstruction on the Suction Seal of the Hip. *Arthroscopy*. 2022 Feb;38(2):365-73.
- Kalhor M, Horowitz K, Beck M, Nazparvar B, Ganz R. Vascular supply to the acetabular labrum. *J Bone Joint Surg Am*. 2010 Nov 3;92(15):2570-5.
- Minokawa S, Naito M, Kinoshita K, Yamamoto T. Acetabular labrum blood flow in developmental dysplasia of the hip: an intraoperative in vivo study using laser Doppler flowmetry. *J Orthop Surg Res*. 2016 Oct 17;11(1):116.
- Aström M, Westlin N. Blood flow in chronic Achilles tendinopathy. *Clin Orthop Relat Res*. 1994 Nov;(308):166-72.
- Christoforetti JJ, Krupp RJ, Singleton SB, Kissenberth MJ, Cook C, Hawkins RJ. Arthroscopic suture bridge transosseus equivalent fixation of rotator cuff tendon preserves intratendinous blood flow at the time of initial fixation. *J Shoulder Elbow Surg*. 2012 Apr;21(4):523-30.
- Schlehr FJ, Limbird TA, Swiontkowski MF, Keller TS. The use of laser Doppler flowmetry to evaluate anterior cruciate blood flow. *J Orthop Res*. 1987;5(1):150-3.
- Nötzli HP, Siebenrock KA, Hempling A, Ramseier LE, Ganz R. Perfusion of the femoral head during surgical dislocation of the hip. Monitoring by laser Doppler flowmetry. *J Bone Joint Surg Br*. 2002 Mar;84(2):300-4.
- Levy O, Relwani J, Zaman T, Even T, Venkateswaran B, Copeland S. Measurement of blood flow in the rotator cuff using laser Doppler flowmetry. *J Bone Joint Surg Br*. 2008 Jul;90(7):893-8.
- Nakashima T, Sone M, Fujii H, Teranishi M, Yamamoto H, Otake H, Sugiura M, Naganawa S. Blood flow to the promontory in cochlear otosclerosis. *Clin Otolaryngol*. 2006 Apr;31(2):110-5.
- Mani R, Cooper C, Kidd BL, Cole JD, Cawley MID. Use of laser Doppler flowmetry and transcutaneous oxygen tension electrodes to assess local autonomic dysfunction in patients with frozen shoulder. *J R Soc Med*. 1989 Sep;82(9):536-8.
- Lindsberg PJ, O'Neill JT, Paakkari IA, Hallenbeck JM, Feuerstein G. Validation of laser-Doppler flowmetry in measurement of spinal cord blood flow. *Am J Physiol*. 1989 Aug;257(2 Pt 2):H674-80.
- Kowalski MJ, Schemitsch EH, Kregor PJ, Senft D, Swiontkowski MF. Effect of periosteal stripping on cortical bone perfusion: a laser Doppler study in sheep. *Calcif Tissue Int*. 1996 Jul;59(1):24-6.
- Swiontkowski MF, Senft D. Cortical bone microperfusion: response to ischemia and changes in major arterial blood flow. *J Orthop Res*. 1992 May;10(3):337-43.

35. Swiontkowski MF, Schlehr F, Sanders R, Limbird TA, Pou A, Collins JC. Direct, real time measurement of meniscal blood flow. An experimental investigation in sheep. *Am J Sports Med.* 1988 Sep-Oct;16(5):429-33.
36. Swiontkowski MF, Tepic S, Perren SM, Moor R, Ganz R, Rahn BA. Laser Doppler flowmetry for bone blood flow measurement: correlation with microsphere estimates and evaluation of the effect of intracapsular pressure on femoral head blood flow. *J Orthop Res.* 1986;4(3):362-71.
37. Nwachukwu BU, Alpaugh K, McCormick F, Martin SD. All-Arthroscopic Reconstruction of the Acetabular Labrum by Capsular Augmentation. *Arthrosc Tech.* 2015 Mar 23;4(2):e127-31.
38. Kucharik MP, Abraham PF, Nazal MR, Varady NH, Meek WM, Martin SD. Minimum 2-Year Functional Outcomes of Patients Undergoing Capsular Autograft Hip Labral Reconstruction. *Am J Sports Med.* 2021 Aug;49(10):2659-67.
39. Syed HM, Martin SD. Arthroscopic acetabular recession with chondrolabral preservation. *Am J Orthop (Belle Mead NJ).* 2013 Apr;42(4):181-4.
40. Kelly BT, Shapiro GS, Digiovanni CW, Buly RL, Potter HG, Hannafin JA. Vascularity of the hip labrum: a cadaveric investigation. *Arthroscopy.* 2005 Jan; 21(1):3-11.
41. Shindle MK, Voos JE, Nho SJ, Heyworth BE, Kelly BT. Arthroscopic Management of Labral Tears in the Hip. *J Bone Joint Surg Am.* 2008;90(Supplement_4): 2-19.
42. Petersen W, Petersen F, Tillmann B. Structure and vascularization of the acetabular labrum with regard to the pathogenesis and healing of labral lesions. *Arch Orthop Trauma Surg.* 2003 Jul;123(6):283-8.
43. Alter T, Beck EC, Mehta N, Cancienne JM, Sarmast S, Liu JN, Nho SJ. Reconstruction Guide for the Measurement of Segmental Labral Insufficiency: An Alternative Technique for Acetabular Labral Reconstruction. *Arthrosc Tech.* 2019 Feb 4; 8(3):e223-9.
44. Espinosa N, Rothenfluh DA, Beck M, Ganz R, Leunig M. Treatment of Femoro-Acetabular Impingement: Preliminary Results of Labral Refixation. *J Bone Joint Surg Am.* 2006;88(5):925-35.
45. Kelly BT, Weiland DE, Schenker ML, Philippon MJ. Arthroscopic labral repair in the hip: surgical technique and review of the literature. *Arthroscopy.* 2005 Dec; 21(12):1496-504.
46. Philippon MJ, Schenker ML. A new method for acetabular rim trimming and labral repair. *Clin Sports Med.* 2006 Apr;25(2):293-7, ix.
47. Skelley NW, Conaway WK, Martin SD. "In-Round" Labral Repair After Acetabular Recession Using Intermittent Traction. *Arthrosc Tech.* 2017 Oct 9;6(5): e1807-13.
48. Blankenbaker DG, De Smet AA, Keene JS, Fine JP. Classification and localization of acetabular labral tears. *Skeletal Radiol.* 2007 May;36(5):391-7.
49. Nötzli HP, Swiontkowski MF, Thaxter ST, Carpenter GK 3rd, Wyatt R. Laser Doppler flowmetry for bone blood flow measurements: helium-neon laser light attenuation and depth of perfusion assessment. *J Orthop Res.* 1989;7(3): 413-24.
50. Nilsson GE, Tenland T, Oberg PA. Evaluation of a laser Doppler flowmeter for measurement of tissue blood flow. *IEEE Trans Biomed Eng.* 1980 Oct;27(10): 597-604.
51. Beaulé PE, Campbell P, Shim P. Femoral head blood flow during hip resurfacing. *Clin Orthop Relat Res.* 2007 Mar;456(456):148-52.
52. Alpaugh K, Shin SR, Martin SD. Intra-articular Fluid Distension for Initial Portal Placement During Hip Arthroscopy: The "Femoral Head Drop" Technique. *Arthrosc Tech.* 2015 Jan 19;4(1):e23-7.
53. McCormick F, Alpaugh K, Nwachukwu BU, Xu S, Martin SD. Effect of radiofrequency use on hip arthroscopy irrigation fluid temperature. *Arthroscopy.* 2013 Feb; 29(2):336-42.
54. Conaway WK, Martin SD. Puncture Capsulotomy During Hip Arthroscopy for Femoroacetabular Impingement: Preserving Anatomy and Biomechanics. *Arthrosc Tech.* 2017 Nov 27;6(6):e2265-9.
55. Eberlin CT, Kucharik MP, Abraham PF, Nazal MR, Conaway WK, Varady NH, Martin SD. Puncture Capsulotomy Technique for Hip Arthroscopy: Midterm Functional Outcomes. *Orthop J Sports Med.* 2023 Jan 26;11(1):23259671221144056.
56. Miyake S, Izaki T, Arashiro Y, Kobayashi S, Shibata Y, Shibata T, Yamamoto T. Excessively High Repair Tension Decreases Microvascular Blood Flow Within the Rotator Cuff. *Am J Sports Med.* 2022 Nov;50(13):3643-8.
57. Harris WH, Bourne RB, Oh I. Intra-articular acetabular labrum: a possible etiological factor in certain cases of osteoarthritis of the hip. *J Bone Joint Surg Am.* 1979 Jun;61(4):510-4.
58. Ganz R, Parvizi J, Beck M, Leunig M, Nötzli H, Siebenrock KA. Femoroacetabular impingement: a cause for osteoarthritis of the hip. *Clin Orthop Relat Res.* 2003 Dec; (417):112-20.
59. Cvetanovich GL, Chalmers PN, Levy DM, Mather RC 3rd, Harris JD, Bush-Joseph CA, Nho SJ. Hip Arthroscopy Surgical Volume Trends and 30-Day Postoperative Complications. *Arthroscopy.* 2016 Jul;32(7):1286-92.
60. Nicholls RL, Green D, Kuster MS. Patella intraosseous blood flow disturbance during a medial or lateral arthrotomy in total knee arthroplasty: a laser Doppler flowmetry study. *Knee Surg Sports Traumatol Arthrosc.* 2006 May;14(5):411-6.
61. Philippon MJ, Arnoczky SP, Torrie A. Arthroscopic repair of the acetabular labrum: a histologic assessment of healing in an ovine model. *Arthroscopy.* 2007 Apr;23(4):376-80.
62. Riley RD, Snell KIE, Ensor J, Burke DL, Harrell FE Jr, Moons KGM, Collins GS. Minimum sample size for developing a multivariable prediction model: Part I - Continuous outcomes. *Stat Med.* 2019 Mar 30;38(7):1262-75.
63. Harrell FE Jr, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med.* 1996 Feb 28;15(4):361-87.