Systematic Review

Radiofrequency-Based Chondroplasty Creates a Precise Area of Targeted Chondrocyte Death With Minimal Necrosis Outside the Target Zone: A Systematic Review

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Purpose: To systematically examine the effects of radiofrequency (RF) ablation or coblation (controlled ablation) on chondrocyte viability following knee chondroplasty in preclinical literature to determine the effectiveness and safety of RF-based techniques. **Methods:** A literature search was performed in September 2022 using PubMed and Scopus using the following search terms combined with Boolean operators: "chondroplasty," "radiofrequency," "thermal," "knee," "chondral defect," "articular cartilage," and "cartilage." The inclusion criteria consisted of preclinical studies examining the effect of RF ablation or coblation on chondrocytes during knee chondroplasty. Exclusion criteria consisted of studies reporting chondroplasty in joints other than the knee, clinical studies, in vitro studies using animal models, case reports, non–full-text articles, letters to editors, surveys, review articles, and abstracts. The following data were extracted from the included articles: author, year of publication, chondral defect location within the knee and chondral characteristics, RF probe characteristics, cartilage macroscopic description, microscopic chondrocyte description, and extracellular matrix characteristics. **Results:** A total of 17 articles, consisting of 811 cartilage specimens, were identified. The mean specimen age was 63.4 ± 6.0 (range, 37-89) years. Five studies used monopolar RF devices, 7 studies used bipolar RF devices, whereas 4 studies used both monopolar and bipolar RF devices. Time until cell death during ablation at any power was reported in 5 studies (n = 351 specimens), with a mean time to cell death of 54.4 seconds (mean range, 23.1-64) for bipolar RF and 56.3 seconds (mean range, 12.5-64) for monopolar RF devices. Chondrocyte cell death increased with increased wattage, while treatment time was positively correlated with deeper cell death. **Conclusions:** In this systematic review, histologic analysis demonstrated that RF-based chondroplasty creates a precise area of targeted chondrocyte death, with minimal evidence of necrosis outside the target zone. Caution must be exercised when performing RF-based chondroplasty due to the risk of cell death with increased application time and wattage. **Clinical Relevance:** Although RF ablation has demonstrated favorable results in preliminary trials, including smoother cartilage and less damage to the surrounding healthy tissue, the risks versus benefits of the procedure are largely unknown. Caution must be exercised when performing RF-based chondroplasty in the clinical setting due to the risk of cell death with increased application time and wattage.

Three-fourths of all cartilage procedures of the knee are performed in the United States.[1-3] Intra-articular chondral lesions in the knee are commonly observed in nearly two-thirds of patients undergoing arthroscopic knee surgery. Chondral defects may inhibit normal knee kinematics, resulting in substantial pain and morbidity, leading to disability and adversely affecting the quality of life.[4,5] Untreated chondral

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defects may progress and enlarge, resulting in the development of early-onset osteoarthritis.[6-8] In the setting of failed nonoperative treatment, operative management may be indicated in the setting of symptomatic chondral lesions, with arthroscopic chondroplasty serving as the most common intervention.[2] By removing loose and fibrillated articular cartilage, surgeons use this technique to stabilize the defect, smoothing the chondral surface of the knee and decreasing the risk for lesion progression.[2]

Chondroplasty encompasses a spectrum of techniques. Historically, arthroscopic mechanical debridement and abrasion of chondral lesion has been used frequently to debride the unstable cartilage down to a stable rim.[9] However, this technique may lead to iatrogenic damage of adjacent healthy tissue, induce localized chondrocyte death, and result in potential disease progression.[10,11] Furthermore, mechanical chondroplasty methods have been reported to result in poor-to-moderate clinical outcomes, with no effect on the treatment of arthrosis.[12,13] Instead, the instrument itself may cause a "tearing" effect on the cartilage, producing wrinkles and grooves, failing to smoothen the articular surface.[14] Meanwhile, it has been postulated that radiofrequency (RF) ablation may address this inadequacy, with favorable results in preliminary clinical trials.[15,16] Unlike ablative laser treatments, which remove the top layer of skin, nonablative RF treatments target deeper layers of the skin without damaging the surface. During nonablative RF treatment, a device with a specialized handpiece is applied to the skin, emitting RF waves that penetrate the skin to heat up the underlying tissue.[17] Thermal energy from an electrosurgical wand causes vaporization of the organic bonds in cartilaginous tissue, allowing for a sealing of the chondral surface with more accurate salvage of healthy chondrocytes.[18] However, chondrocytes are also at risk for damage and necrosis.[6,13,19]

The purpose of this study was to systematically examine the effects of RF ablation or coblation (controlled ablation) on chondral smoothness and chondrocyte viability following knee chondroplasty in preclinical literature to determine the effectiveness and safety of RF-based techniques. The authors hypothesized that RF ablation would be safe and effective in smoothing chondral surfaces.

Methods

Search Strategy

A systematic review was conducted according to the 2020 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines (Fig 1).[20] An independent comprehensive database search was conducted by 2 independent authors (G.J., A.H.) using PubMed and Scopus databases on September 9, 2022. The following search terms with Boolean operators were used: ((thermal) AND (chondroplasty) AND (knee)) OR ((radiofrequency) AND (chondral defect) OR (articular cartilage) OR (cartilage)).

Eligibility Criteria

The inclusion criteria consisted of preclinical studies published in English or with English-language translation, examining the effect of RF ablation or coblation on chondrocyte smoothness and viability during knee chondroplasty, including both monopolar and bipolar RF devices. Exclusion criteria consisted of studies reporting chondroplasty in joints other than the knee, clinical studies, in vitro studies using animal models, case reports, non–full-text articles, letters to editors, surveys, review articles, and abstracts.

Data Extraction

Article eligibility was assessed beginning with initial title and abstract screening, followed by a full-text review performed by 2 independent reviewers (L.S., A.H.). All references included in the eligible studies were reviewed and assessed for eligibility to optimize the identification of all relevant literature.

The following data were extracted from the included articles: author, year of publication, chondral defect location within the knee and chondral characteristics, RF probe characteristics, cartilage macroscopic description, microscopic chondrocyte description, and extracellular matrix characteristics. RF ablation was termed "safe" if the procedure had a low risk of serious complications with minimal death to surrounding healthy tissue, when performed by trained orthopaedic surgeons.

Risk of Bias

Quality and risk of bias of included studies were determined by using the Newcastle–Ottawa Scale (NOS). Eligible studies were independently rated by 2 independent authors, with discrepancies greater than 2 points resolved by a third author (V.G., C.M.). The NOS contains 9 categories related to methodologic quality, with each study eligible for a maximum score of 9 points. The breakdown of specific categories for each of the included studies can be seen in Appendix Table 1, available at www.arthroscopyjournal.org.

Results

Following the initial search, a total of 891 articles were identified, with 570 remaining after duplicate removal. Title and abstract screening resulted in 50 remaining articles. Following full-text review, a total 17 articles were identified as meeting eligibility criteria and were included in the analysis (Fig 1). The range on the NOS was 5-9 with an average score of 7.7.

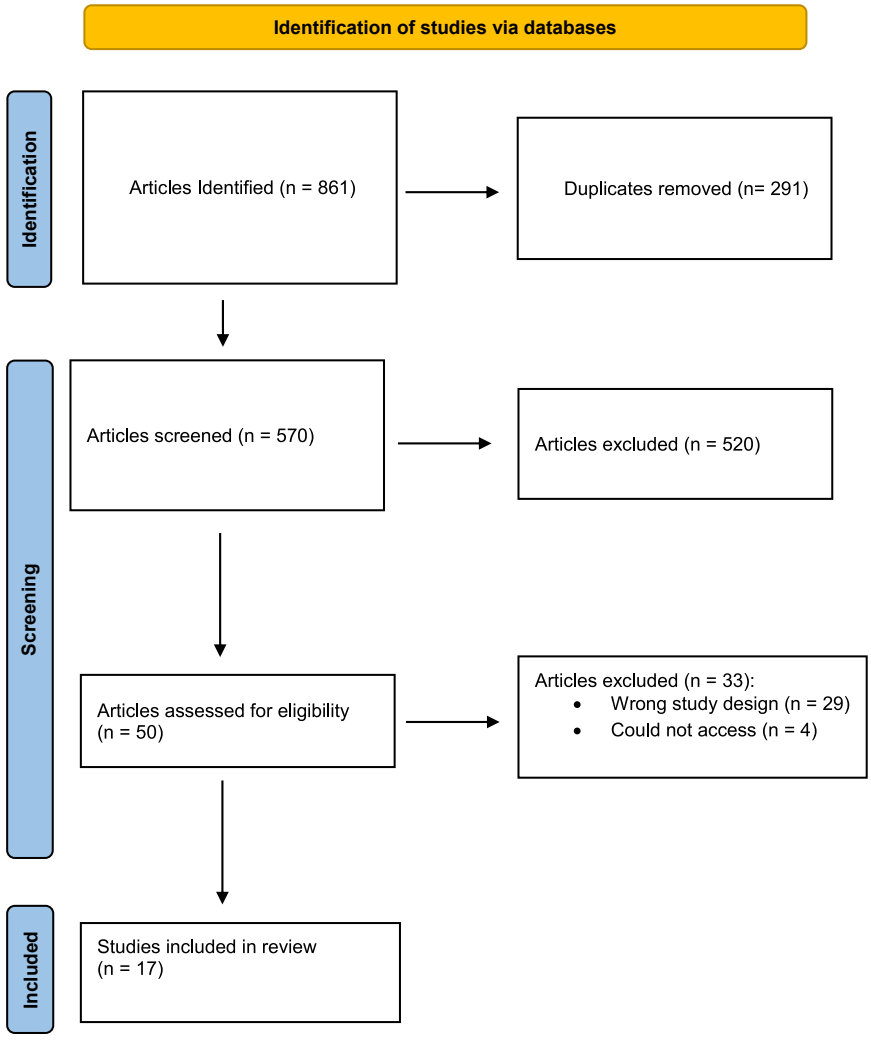

Fig 1. The Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram.

Of the 17 articles, a total of 811 live ex vivo or in vitro cartilage samples were reported, with a mean specimen age of 63.4.3 ± 6.0 (range, 20-89) years (Table 1).[16-18,21-35] The most common Outerbridge classification of the treated cartilage samples was grade 2 (71%, n = 12/17 studies). Five studies[21-25] (n = 195 specimens) used monopolar RF devices, 7 studies[16,26-31] (158 specimens) used bipolar RF devices, whereas 4 studies[17,32-34] (412 specimens) used both monopolar and bipolar RF devices. One study[17] (28 specimens) used a nonablative RF device (Table 2).[16-18,21-35] The most common monopolar RF device used was the Vulcan Electrothermal Arthroscopy System (EAS; Oratec Interventions Inc., Menlo Park, CA) with a temperature-controlled (TAC) probe (293 specimens), whereas the most common bipolar RF device used was the ArthoWand (ArthroCare Corporation, Sunnyvale, CA) (298 specimens). Energy settings ranged from 7 watts to 80 watts. A probe temperature of 70°C was used in 53% (n = 9/17 studies; 567 specimens) of studies with a range of 50° to 160°C. In 64.3% (n = 10/17 studies; 299 specimens) of studies, contact of the RF probe was made directly on the cell surface. One study[32] (124 specimens) applied the probe 1 mm from the cell surface, whereas another study[33] (96 specimens) applied the probe at 0.5 mm from the cell surface.

Eight studies[17,18,22,26,27,29,31,35] (n = 286 specimens) reported on the impact of treatment time or depth for chondral lesions treated following RF-based chondroplasty (Table 2). Caffey et al.[32] observed cell death with increased probe application time. Huang et al.[28] reported that chondrocyte death was significantly greater in the 4°C solutions compared with the 37°C solution. There was a broad range in depth of cell death. Kaplan and Uribe[35] reported a short depth of cell death at 120 microns with the ArthroCare Bipolar probe, whereas Lu et al.[30] reported the depth at 2445 microns with the ArthroCare 2000 coupled with an ArthroCare CoVac probe. For reference, the average thickness of

Table 1. Specimen Demographics

Study	Cartilage Source	Number of Samples	Outerbridge Classification	Mean Age, y (Range)
Caffey et al., 2005[32]	Distal posterior femoral condyle	124	Grades 2 and 3	(57-72)
Cook et al., 2004[33]	Patella, femoral condyle	240	Grade 1 or grade 2/3	–
Dutcheshen et al., 2012[26]	Femoral condyle	50	Grades 2 and 3	63.3 (49-89)
Edwards et al., 2002[18]	Patella, Femoral condyle	30	ArthroCare group: 2.1 ± 0.3 VAPR: 2.2 ± 0.4 Vulcan EAS: 2.2 ± 0.4	ArthroCare group: 64 ± 8 VAPR: 67 ± 11 Vulcan EAS: 66 ± 7
Enochson et al., 2012[27]	Unspecified knee	12	–	(38-49)
Ganguly et al., 2012[17]	Femoral condyle, tibial plateau, patella	28	–	59
Huang et al., 2014[28]	Femoral condyle	28	Grades 1 and 2	65
Kang et al., 2008[22]	Femoral condyle	15	Grades 2 and 3	50 (35-69)
Kaplan and Uribe, 2000[35]	Femoral condyle	6	–	–
Lotto et al., 2008[25]	Patella	48	Grades 2 and 3	–
Lu et al., 2001[30]	Femoral condyle or patella	ArthroWand: 12 CoVac 50°: 12	Grades 2 and 3	62
Lu et al., 2002 (Lavage)[23]	Unspecified knee	22°C lavage: 16 37°C lavage: 16	Grade 2	65
Lu et al., 2002[34]	Unspecified knee	Vulcan EAS: 36 ArthroCare 2000: 36	Grade 2	Vulcan EAS: 64 ArthroCare 2000: 61
Meyer et al., 2005[24]	Unspecified knee	30	Grades 2 and 3	–
Owens et al., 2002[31]	Patella	20	Grades 2 and 3	36.9
Spahn et al., 2008[16]	Femoral condyle	30	–	42.9 (20–57)
Yasura et al., 2006[21]	Unspecified knee	86	–	71

NOTE. Vulcan EAS (Oratec Interventions Inc., Menlo Park, CA); VAPR (Mitek Corporation, Norwood, MA) ArthroCare 2000, ArthoWand and CoVac probe (ArthroCare Corporation, Sunnyvale, CA).

cartilage in condyle tissue can vary depending on several factors, including age, sex, weight, and activity level. However, in general, the average thickness of healthy knee cartilage is approximately 2000 and 3000 microns.[36] With both studies using identical energy settings, this difference in cell death could potentially be the distance of probe application to cell surface. Cell death increased with increase wattage used in both studies.[30,35] Treatment time was positively correlated with deeper cell death.[28]

Microscopic analysis of the extracellular matrix (ECM) following RF-based chondroplasty was reported in 4 studies[17,18,27,35] (n = 92 specimens) (Table 3).[17,18,21,23,23-25,27,28,30,33-35] Edwards et al.[18] observed reduced proteoglycan staining of the ECM in 30 specimens. Reduced proteoglycan staining may be an indication of tissue damage or dysfunction. Huang et al.[28] (28 specimens) reported flake cell death in regions treated with the RF probe. Flake cell death, also known as chondroptosis, or apoptosis of chondrocytes, is a type of cell death that occurs in cartilage tissue. Ganguly et al.[17] (28 specimens) found contraction of the ECM in the superficial zone and regions continuous to the removed cartilage.

Four studies[21,26,33,35] (382 specimens) reported on collagen description with the use of staining methods. Three studies[21,26,33] (328 specimens) reported a decrease in type II collagen content following RF treatment. The authors of one study[22] (6 specimens) found no evidence of collagen degeneration in the treated areas compared with the untreated areas. There were contradictory reports between the 3 studies that included changes in matrix metalloprotease 13 levels after RF treatment.[3,27,33]

Discussion

The main finding of this investigation is that RF-based chondroplasty induces duration and wattage-dependent chondrocyte necrosis in a well-targeted area without significant collateral damage. Histologic analysis demonstrated RF-based chondroplasty to create a precise area of targeted chondrocyte death, with minimal evidence of necrosis outside the target zone. However, this was not clear in all studies due to lack of appropriate control group.

The most used probe temperature for treatment was 70°C, with 2 studies[30,34] using probe temperatures greater than 100°C. The treatment temperature is in line with previous studies that reported a temperature of at least 65°C being necessary to alter collagen in the shoulder.[29] However, chondrocyte necrosis can occur at 50 to 55°C, which may delay healing.[37] Most studies applied the probe for less than 30 seconds. However, Kaplan and Uribe[35] and Lu et al.[30] applied the probe for under 3 seconds, while the ORATEC treatment group in Edwards et al.[18] applied the probe for an average of 39 seconds. The literature has found that significant changes in cartilage histology can occur with small differences in probe application time. Specifically, Lakshmi et al.[38] reported significant differences in cartilage fibrosis, chondrocyte clustering, and proteoglycan content following the application of RF in 1-, 3-,

Table 2. RF Device Characteristics and Depth of Chondral Damage

Study	RF Device	RF Polarity	Energy Setting, Watts	Probe Temperature, °C	Time of application, s	Distance of Probe Application to Cell Surface	Depth of Death, microns
Caffey et al., 2005[32]	ACD 50 probe; Temperature Control Electrode; Ultrablator 2.5-mm; Vulcan TAC-CII; Serf 90	Monopolar: Ultrablator Bipolar: ACD 50, Temperature Control Electrode, Vulcan TAC-CII, Serf 90	ACD 50: 3 Temperature Control Electrode: 40 Ultrablator 2.5-mm probe: 40 Vulcan TAC-CII: 15 Serf 90: coagulation medium	ACD 50 probe: — Temperature Control Electrode setting: 55°C Ultrablator 2.5-mm probe: –Vulcan TAC-CII: 70° Serf 90: coagulation medium	1, 3	On surface and 1 mm off surface	ACD 50 probe: 1 s: 404 3 s: 1034 Temperature Control Electrode: 1 s: 45 3 s: 1048 Ultrablator 2.5-mm probe 1 s: 521 3 s: 1283 Vulcan TAC-CII: 1 s: 539 3 s: 1242 Serf 90: not able to differentiate from control
Cook et al., 2004[33]	Vulcan EAS; VAPR II	Monopolar: Vulcan EAS Bipolar: VAPR II	15 and 30	Vulcan EAS: 70°C VAPR II: —	—	Vulcan EAS: contact VAPR II: 0.5mm	—
Dutcheshen et al., 2012[26]	Paragon T2	Bipolar	Power setting 7	50°C	45	—	Cartilage thickness decreased by a mean of 15.91%
Edwards et al., 2002[18]	ArthroCare; VAPR; Vulcan EAS	Bipolar: ArthroCare, VAPR Monopolar: Vulcan EAS	ArthroCare: Setting 2 VAPR: Setting V2-40 Vulcan EAS: 30	Vulcan EAS: 70°C Other Probes: —	ArthroCare: 24.2 ± 9.0 VAPR: 23.1 ± 6.9 Vulcan EAS: 39 ± 18.5	—	ArthroCare: 2228 VAPR: 2810 Vulcan EAS: 737
Enochson et al., 2012[27]	Paragon T2 probe	Bipolar	Level 6 (equal to 234V ± 10%)	—	—	On surface	Reached 150- to 200-μm deep in both alginate gels and biopsy specimens
Ganguly et al., 2012[17]	Nonablation RF device	—	25 with 8500-V peak-to-peak setting (4250 peak voltage) and 390-kHz damped sinusoid bursts with a repetition frequency of 30 kHz into 500 ohms	—	—	—	—

(continued)

Table 2. Continued

Study	RF Device	RF Polarity	Energy Setting, Watts	Probe Temperature, °C	Time of application, s	Distance of Probe Application to Cell Surface	Depth of Death, microns
Huang et al., 2014[28]	Bipolar RF with ArthroCare TriStar 50 and Paragon T2 probes	Bipolar	Treatment power of level 2, 4, and 6	—	2, 5, 10	Light contact	2 s: 298 5 s: 420 10 s: 608
Kang et al., 2008[22]	Vulcan EAS 3.12 with TAC-C probe	Monopolar	30	70	14.1	Light contact	—
Kaplan and Uribe, 2000[35]	ArthroCare multielectrode 3-mm wand	Bipolar	Three settings used S2: 133-147 kHz (low) S4: 160-179 kHz (mid) S6: 190-210 kHz (high)	—	3	Light contact	Depth of Tissue Removal: S2: 0.12 mm S4: 0.23 mm S6: 0.37 mm
Lotto et al., 2008[25]	Dyonics Glider Articular Cartilage Probe and Vulcan EAS generator, 3.71	Monopolar	60	—	—	On surface	First pass: 150 Second pass: 150 Third pass: 150 Fifth pass: 50 10th pass:
Lu et al., 2001[30]	ArthroCare 2000 with a 3mm 90° ArthroWand or CoVac 50° angle probe	Bipolar	Three settings used S2: 133-147 kHz (low) S4: 160-179 kHz (mid) S6: 190-210 kHz (high)	ArthroWand: 100-160 CoVac 50°: 70	3	No contact (1 mm above surface)	ArthroWand S2: 1,512 S4: 1,886 S6: 2,269 CoVac 50° S2: 1,929 S4: 2,193 S6: 2,445
Lu et al., 2002 (Lavage)[23]	TAC-C II probe	Monopolar	15	70	10, 15	Light contact (paintbrush treatment pattern)	10 s, 22°C lavage: 620 10 s, 37°C lavage: 420 15 s, 22°C lavage: 930 15 s, 37°C lavage: 590
Lu et al., 2002[34]	Vulcan EAS coupled with a TAC-C probe ArthroCare 2000 with ArthroCare CoVac 50° angle probe	Monopolar: Vulcan EAS Bipolar: ArthroCare 2000	15	Vulcan EAS: 70 ArthroCare 2000: 100-110	5, 10, 15, 20, 30, 40	Vulcan EAS: Light contact ArthroCare 2000: No contact (1 mm above surface)	Vulcan EAS: 0.79 mm at 15 s ArthroCare 2000: 2.1 mm at 15 s
Meyer et al., 2005[24]	Vulcan EAS	Monopolar	80	—	15	Light contact (paintbrush treatment pattern)	Aluminum nitride: 246 Teflon (PTFE): 231 Partially stabilized zirconia (YTZP): 195 Corning Macor ceramic: 176 99.5% Alumina: 130 Zirconia toughened alumina (ZTA): 114

(continued)

Table 2. Continued

Study	RF Device	RF Polarity	Energy Setting, Watts	Probe Temperature, °C	Time of application, s	Distance of Probe Application to Cell Surface	Depth of Death, microns
Owens et al., 2002[31]	VAPR	Bipolar	20	60-80	–	–	–
Spahn et al., 2008[16]	Paragon	Bipolar	Level 6 (equal to 234V ± 10%)	50	–	–	–
Yasura et al., 2006[21]	Vulcan EAS with TAC-CII probe	Monopolar	15	70	15	Light contact (paintbrush treatment pattern)	–

NOTE. ACD 50 probe (ArthroCare Corporation, Sunnyvale, CA); Temperature Control Electrode (Mitek Products Inc., Westwood, MA); Ultrablator 2.5-mm (Linvatec, Largo, FL); Vulcan TAC-CII (Oratec Interventions Inc., Menlo Park, CA); Serf 90 (Stryker Endoscopy, Santa Clara, CA); Vulcan EAS (Oratec Interventions Inc., Menlo Park, CA); VAPR & VAPR II (Mitek Corporation, Westwood, MA); Paragon T2 (ArthroCare Corporation, Sunnyvale, CA); VAPR (Mitek Corporation, Norwood, MA); Nonablation RF device (NuOrtho Surgical, Fall River, MA); Dyonics Glider Articular Cartilage Probe (Smith & Nephew Endoscopy, Andover, MA), Paragon (ArthroCare Corporation, Austin, TX).
EAS, electrothermal arthroscopy system; RF, radiofrequency.

and 5-second intervals. Given the wide heterogeneity of probe application time in studies included in this review, further investigations are warranted to determine optimal wattage-application time based on device type, distance, power, and chondral defect to achieve effect of chondroplasty while minimizing chondrocyte necrosis. As a result of the time-dependent effect of RF on cell death, when working with larger samples of tissue, it is reasonable to mechanically debride the tissue in order to limit undesired prolonged RF-based effects on the adjacent cartilage and joint fluid which may potentially adversely affect chondrocyte viability.

The histologic appearance of cartilage following RF chondroplasty demonstrates that RF may be a viable treatment option for the treatment of symptomatic chondral defects within the knee. Across all studies, treatment of the cartilage with RF resulted in a smooth surface along with a color change from white to yellow to brown over application time. Ganguly et al.,[17] who used a nonablative device, reported no necrotic tissue was appreciated adjacent to the damaged tissue targeted, indicating that the superficial zones of cartilage remained intact. The microscopic description of the cartilage can demonstrate the accuracy of the RF device in removing cartilage while maintaining the superficial zone. Enochson et al.,[27] Ganguly et al.,[17] and Huang et al.[28] observed well-defined borders in the areas of cartilage targeted for removal with a surrounding superficial zone consisting of undamaged, healthy chondrocytes. This finding contradicts the results reported by Ryan et al.,[39] in which histologic changes in the superficial zone were observed at 60-watt RF application. Furthermore, the deleterious effects of RF-based chondroplasty in the healthy adjacent cartilage found in earlier studies are likely overestimated due to the use of confocal laser microscopy and vital cell staining, as postulated by Kaplan.[40]

Adjacent chondrocyte viability remains high after RF-based chondroplasty. Lu et al.[30] reported normal chondrocyte morphology with visible nuclei after treatment. Additionally, Enochson et al.[27] observed rapid cell proliferation in the 3 days following ablation. After treatment, Yasura et al.[21] found significant reductions in matrix metalloprotease, an enzyme responsible for degenerative changes leading to osteoarthritis.[41] A similar decrease in osteoarthritis biomarkers after RF treatment was reported by Takahashi et al.,[42] who observed a decrease in autophagy biomarkers, Unc-51-like kinase 1, and Beclin1. These findings support the use of RF treatment for the treatment of chondral defects while decreasing the risk for iatrogenic chondrocyte damage and the development of osteoarthritis.

A large degree of heterogeneity is reported in the depth of cell death following RF. The greatest factor affecting the depth of cell death was the use of a

Table 3. Microscopic Findings

Study	Chondrocyte Cell Viability	ECM Description	Cell Appearance/ Distribution	Nuclear Morphology	Collagen Description/ Staining	MMP Immunohistochemistry
Cook et al., 2004[33]	–	RF-treated cartilage had a diminished superficial zone with "sealing" of the articular surface, decreased superficial and intermediate zone proteoglycan staining in all groups	Loss of chondrocyte density and empty lacunae within the superficial zone	–	Type II collagen predominance. All sections had loss of normal type II collagen staining in the superficial and intermediate zones compared with normal articular cartilage	Subjectively more MMP-13 immunoreactivity in cartilage treated with 30 W of bipolar radiofrequency than in all other groups. MMP-13 staining was noted in all zones of the cartilage explants but predominated within the intermediate and deep zones. Immunoreactivity of MMP-13 remained elevated in all radiofrequencies treated cartilage throughout the study period
Edwards et al., 2002[18]	In all samples control cartilage demonstrated viable chondrocytes with no cell death. The bipolar radiofrequency energy devices produced chondrocyte death to a greater depth and smoothed the surface faster than did the monopolar device. Chondrocyte death to the level of the subchondral bone occurred with each bipolar device evaluated but not the monopolar device	Reduced proteoglycan staining in the cartilage regions treated	–	–	–	–
Enochson et al., 2012[27]	Underlying tissue seemed viable and undamaged as determined by the staining. The control samples showed no increase in cell death.	Live/dead staining of the ablation-exposed surfaces showed a well-defined local margin of cell death both in the alginate gels and in the human cartilage biopsy specimens.	–	–	–	No effect could be detected on the matrix-degrading component MMP-13 or the matrix components type II collagen when compared with control

(continued)

Table 3. Continued

Study	Chondrocyte Cell Viability	ECM Description	Cell Appearance/ Distribution	Nuclear Morphology	Collagen Description/ Staining	MMP Immunohistochemistry
Ganguly et al., 2012[17]	Live cells were abundantly observed with only occasional dead cells residing in extruded positions at the frayed margins of the fibrillated tissue. An increase in dead cell populations was not evident in either the 1-hour or the 96-hour treated samples over the untreated sample groups, nor was a decrease in chondrocyte viability observed relative to incubation time.	Axis rotation assessments indicated evidence of qualitative extracellular matrix contraction in the tissue immediately contiguous to the tissue targeted for removal and within the superficial zone region when compared to untreated samples	Cells typically contained a large nucleus with loosely packed euchromatin and denser heterochromatin. Homogeneous staining intensities appeared uniform in the z-axis compressed images	The serial tomographic images demonstrated no evidence of altered nuclear morphology when compared with untreated samples. Nuclear fragmentation or condensation was not present within the tissue chondrocytes subadjacent to the tissue targeted for removal, reflecting no evidence of chondrocyte apoptosis. Occasional single randomly positioned cells demonstrated altered nuclear morphologies in some untreated and treated samples, which could not be linked to the treatment site and likely represented fixation-dependent or other causes typical within articular cartilage	—	—

(continued)

Table 3. Continued

Study	Chondrocyte Cell Viability	ECM Description	Cell Appearance/ Distribution	Nuclear Morphology	Collagen Description/ Staining	MMP Immunohistochemistry
Huang et al., 2014[28]	A defined margin of chondrocyte death under controlled conditions and the depth of in situ dead chondrocytes at 37°C was significantly less than those at 22°C ($P = .013$) and 4°C ($P = .001$). The percentage of cell death was the lowest in a 37°C solution and the greatest in a 4°C solution ($P = .003$)	Thermal injury from the ArthroCare TriStar 50 radiofrequency energy showed that the flake cell death of cartilage was frequently appeared regionally in the central zone of the thermal injury. The dead cell spread to the surrounding area, which appeared as a small area of living and dead cells. Laser confocal microscopy projections demonstrated that articular cartilage below the treatment site was void of living chondrocytes. Each treatment site yielded a well-demarcated border between the chondrocytes brightly stained with green and an area of red just above the border	—	—	—	—
Kaplan and Uribe, 2000[35]	The chondrocytes were viable in the tissue adjacent to the treatment site	There were no histopathological differences among the sites subjected to different voltage settings. No differences in collagen birefringence to polarized light on the unstained deparaffinized specimens between the treated and untreated areas. (i.e., the fibrillar component of the matrix remains unaltered by the procedure). No evidence of collagen degeneration	—	No alterations in nuclear, cytoplasmic, nor surrounding lacunar structure when compared with uninjured untreated and injured areas	Hematoxylin & eosin, Periodic acid—Schiff, Alcian blue, colloidal iron, Gomori trichrome, elastic Van Gieson	—

(continued)

Table 3. Continued

Study	Chondrocyte Cell Viability	ECM Description	Cell Appearance/ Distribution	Nuclear Morphology	Collagen Description/ Staining	MMP Immunohistochemistry
Lotto et al., 2008[25]	–	At a Wattage setting of 60 or greater, a char-like layer was observed. This char-like layer was associated with a lesser degree of cell death.	–	–	–	–
Lu et al., 2001[30]	CLM showed both probes created immediate chondrocyte death with the demarcation of thermal injury clearly present and in some specimens reaching subchondral bone	Safranin-O staining was weaker (lighter orange in color) within the superficial layer of treated cartilage with a clear demarcation visualized between treated and untreated regions	–	Chondrocyte nuclei were present within treated regions and not different in appearance from sham-operated cartilage and adjacent untreated regions. No alterations in chondrocyte nuclei and surrounding lacunar structure in treated region with both wands	Hematoxylin and eosin, Safranin-O, CLM	–
Lu et al., 2002 (Lavage)[23]	–	–	–	–	CLM	–
Lu et al., 2002[34]	–	–	–	–	CLM	–
Meyer et al., 2005[24]	–	–	–	–	CLM	–
Yasura et al., 2006[21]	–	–	–	–	Safranin O revealed smoothed contouring from thermal application, but there was reduced type II collagen in RFE treated samples	Significant reductions in MMP amounts

CLM, confocal laser microscopy; ECM, extracellular matrix; MMP, matrix metalloproteinase; RF, radiofrequency; RFE, radiofrequency energy.

monopolar or bipolar RF device, the latter of which is reported to reach a depth close to 3-fold to that of the former.[17,22,30] Lu et al.[30] were the only authors to report the width of cell death, ranging from 4,188 to 5,314 microns depending on the setting. Based on these results, bipolar devices are more effective at promoting cell death and penetrating to the subchondral bone than their monopolar counterparts. In addition, bipolar RF is believed to generate a greater annealing effect, meaning decreased permeability of the cartilage and, thus, retaining the compressive stiffness attributed to the water component of the chondral tissue.[43] Nevertheless, there is a possible tradeoff with decreased cartilage smoothness with bipolar relative to monopolar RF,[23] demonstrating the need to optimize RF devices to specific chondral defects. Furthermore, the increased penetration to the subchondral bone from bipolar RF may potentially increase the risk of osteonecrosis following RF-based chondroplasty—although a systematic review of clinical studies by Kosy et al.[14] reported a low rate of osteonecrosis irrespective of probe design.

Limitations

This study is not without limitations. Although RF devices show promising results in preclinical models, the in vitro nature of the included studies prohibits the assessment of the clinical applicability and safety regarding the use of RF for the treatment of chondral lesions in the knee. Furthermore, the high heterogeneity in RF techniques is another significant limitation, limiting the ability to determine optimal outcomes based on RF type, energy setting, temperature and time. In addition, the qualitative nature of the microscopic and macroscopic histologic cartilage descriptions makes a direct, quantitative comparison between studies difficult. As such, no meaningful statistical analysis could be performed to analyze how the time of application, power, and distance affected the depth of cell death.

Conclusions

In this systematic review, histologic analysis demonstrated that RF-based chondroplasty creates a precise area of targeted chondrocyte death, with minimal evidence of necrosis outside the target zone. Caution must be exercised when performing RF-based chondroplasty due to the risk of cell death with increased application time and wattage.

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Appendix Table 1. A Methodologic Quality Assessment of the Included Studies Using the Newcastle–Ottawa Scale

	Selection					Comparability	Outcome			
Study	Representativeness of Treated Cohort	Selection of Comparative Cohort	Ascertainment of Treated Cohort	Outcome Of Interest Was Not Present at Start	Controls for Age/Sex	Controls for Any Additional Factor	Assessment of Outcome	Long Enough Follow-Up	Adequacy of Follow-Up	Total Quality Score
Caffey (2005)	1	1	1	1	1	1	1	1	1	9
Cook (2004)	1	1	1	1	0	1	1	1	1	8
Dutcheshen (2012)	1	1	1	1	1	1	0	1	1	8
Edwards (2002)	1	1	1	1	1	1	1	1	1	9
Enochson (2012)	1	1	1	1	1	1	0	1	1	8
Ganguly (2012)	1	1	1	1	1	1	1	1	1	9
Huang (2014)	1	1	1	1	0	1	0	1	1	7
Kang (2008)	1	1	1	1	1	1	1	1	1	9
Kaplan (2000)	1	1	0	1	0	0	0	1	1	5
Lotto (2008)	1	1	1	1	0	0	0	1	1	6
Lu (2001)	1	1	0	1	1	1	1	1	1	8
Lu (2002) (Lavage)	1	1	0	1	1	1	0	1	1	7
Lu (2002)	1	1	1	1	1	1	0	1	1	8
Meyer (2005)	1	1	0	1	0	1	1	1	1	7
Owens (2002)	1	1	0	1	1	1	1	1	1	8
Spahn (2008)	1	1	0	1	1	1	0	1	1	7
Yasura (2006)	1	1	0	1	1	0	0	1	1	6

NOTE. Each study was evaluated on the following: the study groups selected; the groups comparability; and the ascertainment of the outcomes measured. If the study met the requirements for each characteristic, a "1" was assigned. A maximum of 9 points can be awarded to each study.