

Randomized Study

Comparisons of Monopolar Lesion Volumes with Hypertonic Saline Solution in Radiofrequency Ablation: A Randomized, Double-Blind, Ex Vivo Study

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Background: Chronic degeneration of the zygapophyseal joints in the cervical or lumbar spine are common causes of axial back pain. Radiofrequency (RF) ablation is a treatment modality in the denervation of facet joint-related pain. Although multiple factors have been theorized to contribute to the size of the optimal RF lesion, the addition of hypertonic saline solution has been posited to create larger RF lesion sizes.

Objectives: This study compares lesion of 20-gauge RF monopolar probe using 2% lidocaine, 0.9% normal saline solution, and 3% saline solution administered through the RF needle prior to ablation, with subsequent lesion sizes recorded.

Study Design: Randomized, double-blinded, ex vivo study using clinically relevant conditions.

Setting: Procedural laboratory in an academic institution.

Methods: RF ablation lesions were reproduced in room temperature ($21^{\circ}\text{C} \pm 2^{\circ}\text{C}$) chicken breast specimens with 20-gauge monopolar RF probes inserted. RF was applied for 90 seconds at 80°C after injection of 1 mL of either 2% lidocaine, 2% lidocaine and 0.9% normal saline solution in a 1:1 ratio, or 2% lidocaine and 3% saline solution in a 1:1 ratio. Tissues were dissected, measured, and ellipsoid volumes of burn calculated. Homogeneity of variances was assessed via the Bartlett's test, and heteroskedasticity with the studentized Breusch-Pagan test. One-way analysis of variance (ANOVA) (α of 0.05) was used to evaluate statistical significance between volume means across groups. When the null hypothesis of no difference in burn volume between samples could not be rejected, a predefined equivalence volume of $\pm 0.05 \text{ cm}^3$ was used with Welch's 2 one-sided t-tests (TOST) with a Bonferroni adjusted α of 0.0167 to evaluate for null acceptance.

Results: The mean lesion volume for monopolar RF with 1 mL 2% lidocaine was 0.16 cm^3 . Monopolar RF with 1 mL 2% lidocaine + 0.9% normal saline solution had a mean lesion volume of 0.15 cm^3 , and treatment with 1 mL 2% lidocaine + 3% saline solution measured 0.17 cm^3 . ANOVA failed to reject the null, and TOST accepted as equivalent all 3 comparisons.

Limitations: In vivo anatomy and physiology of a human organism was not used for this study. Samples were not warmed to physiologic temperature. Randomization resulted in slightly unequal sample sizes, although all groups were of sufficient size that the central limit theorem should apply.

Conclusions: Three commonly used solutions were found to have equivalent lesion sizes from monopolar probe RF ablation.

Key words: Radiofrequency, ablation, lesion shape, lesion size, monopolar RF, hypertonic saline solution

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Approximately 80% of people will experience some form of back pain in their lifetime, with an annual incidence of 15% of adults experiencing significant and disabling lower back pain (1). Back pain is undoubtedly complex, and it correlates with unique pathological entities and a wide presentation that can exist from multiple coexisting pain generators. Although the majority of back pain syndromes are treated with conservative therapy in the absence of severe features, intervention is reserved for refractory cases (2). Radiofrequency (RF) electrical currents have been used since the 1950s to create thermal lesions of nervous tissue, leading to pain relief (3). RF ablation is a technique that uses fluoroscopic landmarks for optimal positioning of the insulated needle with an active exposed distal tip (4). Once the RF probe is confirmed with anteroposterior imaging, lateral imaging, and sensory and motor testing, high-density RF current is delivered to the surrounding tissue resulting in increased temperature around the active tip.

Thermal lesions created by RF extend outward radially in the shape of an ellipsoid (5).

Many factors can result in a failure to create a lesion, including anatomic variability. Three factors that are in the provider's control are the size of the lesion based on the gauge of the needle, current density, and duration of application of the RF current (6). Additionally, studies have been conducted that experiment with changing the salinity of the injectate solution (7,8). Studies by Provenzano et al (7) using an ex vivo poultry model indicate that sodium chloride concentrations above 0.7% increased lesion surface area in an ex vivo poultry model. In an in vivo porcine model, Provenzano et al (8) found that fluid modulation of the injectate with 8% sodium chloride increased

lesion volume. Although studies that indicate a relationship between lesion size and salinity of solution exist, this has not been explored using conditions more reflective of that used by providers in the clinical setting. Additionally, it is not known if there is a significant increase in 3-dimensional lesion volumes with an increase in saline solution concentration.

This ex vivo study introduced a single variable, which was the salinity of the crystalloid used in conjunction with the local anesthetic. We hypothesized a positive relationship between saline solution concentration and 3-dimensional lesion volume. Monopolar 20-gauge, nonprotruding probes, and duration of lesion of 90 seconds at 80°C were used to view the effects of hypertonic saline solutions on lesion size produced by RF ablation.

METHODS

Chicken breasts were equilibrated to room temperature ($21^{\circ}\text{C} \pm 2^{\circ}\text{C}$) for 1 hour and then cut into 120 cubed samples measuring approximately 3.0 cm a side. The samples were devoid of bones and blood vessels, which may affect lesion size. Treatment groups included the following injectates: 2% lidocaine + 3% saline solution in a 1:1 ratio (group A), 2% lidocaine + 0.9% normal saline solution in a 1:1 ratio (group B), and 2% lidocaine alone (group C). A randomized list of 150 integers was generated that contained either 1, 2, or 3 using an online tool with the treatment groups assigned as A = 1, B = 2, and C = 3 (9). The order of the randomized list was followed during the injection and ablation process. This randomization by the injectate preparer ensured that the treatments were blinded to the injector/ablator, measurer, and statistician until after analysis was complete. For each sample, 1 mL of injectate was delivered by syringe into the center of the tissue by approximation.

RF ablation was performed at the site of injection using a temperature-controlled RF generator, shown in Fig. 1 (RF Multigen 2: REF 8400-000-000, Stryker, Kalamazoo, MI), a 100-mm, 20-gauge, 10-mm curved active tip cannula (Stryker: REF 0406-660-125), and a



Fig. 1. Radiofrequency generator and grounding pad.

100-mm monopolar nitinol electrode (Stryker: REF 8400-825-010). The grounding pad was placed underneath the sample and the probe was inserted parallel to it. Ablation occurred for a duration of 90 seconds at 80°C. The sample was then taken to the measurer who was blinded to all prior activity.

The tissue sample was sliced through the probe entry point to expose the lesion. Radii were calculated by measuring the diameter of the lesion to the nearest 0.10 cm in 3 dimensions: depth (d), transverse (t), and longitudinal (l) and dividing each by 2 (Fig. 2). All measurements were obtained by the same blinded measurer for consistency.

Data Analyses

Mean lesion volume was calculated for the chicken breast samples that comprised a treatment group. Volume was calculated for an ellipsoid using $V = \frac{4}{3}\pi d t l$. Although the treatment groups had slight differences in sample sizes that arose owing to the randomization method, the sample sizes were large enough such that the central limit theorem still applies. Homogeneity of variances was assessed via the Bartlett's test, and heteroskedasticity with the studentized Breusch-Pagan test. One-way analysis of variance (ANOVA) (α of 0.05) was used to evaluate statistical significance between volume means across groups. If the null hypothesis of no difference in burn volume between samples could not be rejected, a predefined equivalence volume of $\pm 0.05 \text{ cm}^3$ was used with Welch's 2 one-sided t-tests (TOST) and a Bonferroni adjusted α of 0.0167 to evaluate for null acceptance across the groups. Analysis was performed in R v.3.5.2 in RStudio v.1.1.123 (Comprehensive R Archive Network, Boston, MA) using packages lmtest and equivalence (10-11).

RESULTS

Summary statistics of each group are shown in Table 1. Figure 3 provides a graphic comparison of lesion volumes for each injectate. The Bartlett test (K-squared = 2.536, df = 2, $P = 0.2814$) and the Breusch-Pagan test (BP = 2.5239, df = 2, $P = 0.2831$) supported significance testing with ANOVA. This ANOVA failed to show significance (df = 2, sum sq = 0.00536, mean sq = 0.002678, F value = 1.403, $\text{Pr}(>F) = 0.25$). As the ANOVA failed to reject the null, TOST was used with the predetermined equivalence range to evaluate the rejection of a null hypothesis of statistical difference. Significance was found in all group comparisons using a Bonferroni adjusted 98.33% confidence interval with P values, as shown in Table 2.

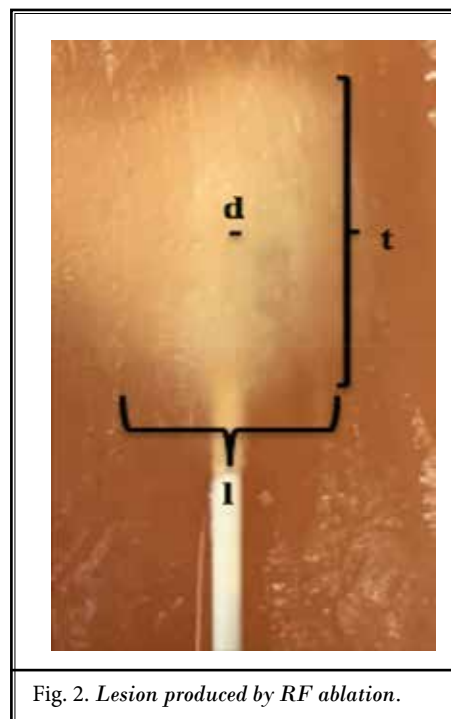


Fig. 2. Lesion produced by RF ablation.

DISCUSSION

RF ablation of the medial branch nerve of the dorsal rami has been the mainstay of treatment of cervical, thoracic, and lumbar spondylosis. RFA lesion size is dictated by 3 factors: the energy delivered to the medial branch nerve, duration of thermal energy, and size of the lesion. The energy and duration of thermal energy applied to the medial branch nerve are modifiable in vivo. As evidence suggests, temperature-time integration is an accurate indicator of lesion size (12). Studies from liver and renal cryoablation or RF therapy procedures with bipolar technology have displayed well-delineated necrotic lesions with

Table 1. Summary statistics of lesion diameters and volumes.

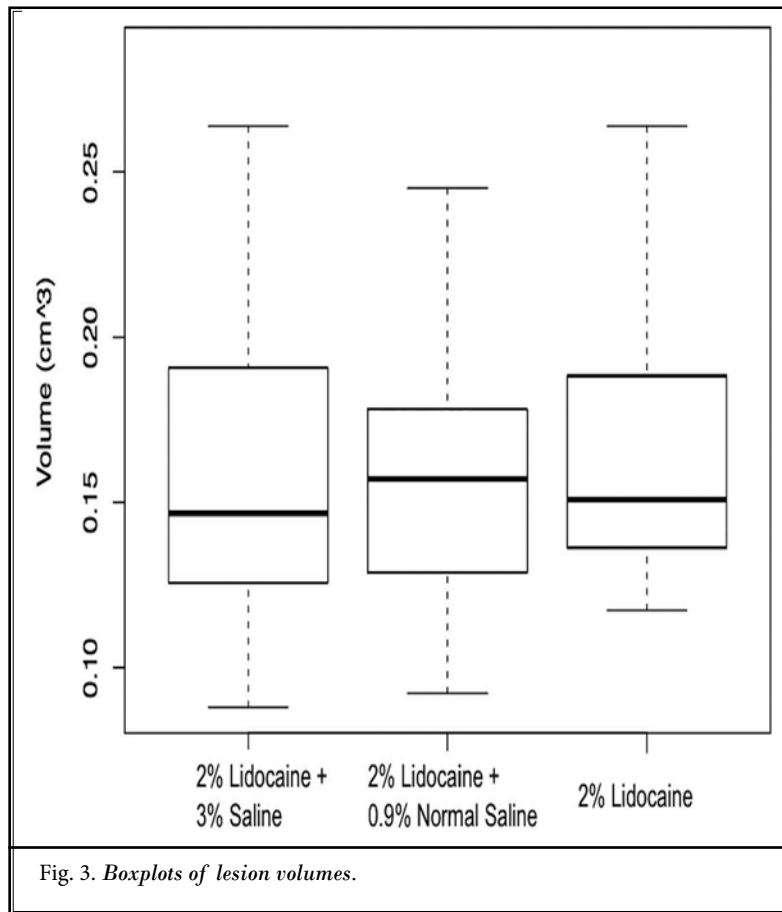
	Group A (n = 39)	Group B (n = 38)	Group C (n = 43)
Depth (cm)	0.49 ± 0.08	0.45 ± 0.07	0.47 ± 0.07
Transverse (cm)	1.27 ± 0.11	1.31 ± 0.14	1.29 ± 0.14
Longitudinal (cm)	0.52 ± 0.07	0.50 ± 0.08	0.50 ± 0.07
Volume (cm ³)	0.17 ± 0.05	0.15 ± 0.05	0.16 ± 0.04

*Group A was treated with 2% lidocaine + 3% saline, group B with 2% lidocaine and 0.9% normal saline, and group C with 2% lidocaine.

Table 2. *Welch 2 sample TOST.*

Groups*	df	98.33% CI Low	98.33% CI High	P-value
A & B	74.979	-0.007388196	0.038817548	0.000959
A & C	72.027	0.1704381	0.1580051	9.60E-05
B & C	71.738	-0.02361371	0.01705046	2.09E-06

*Group A was treated with 2% lidocaine + 3% saline, group B with 2% lidocaine and 0.9% normal saline, and group C with 2% lidocaine.



According to our statistical analysis. This ex vivo study demonstrates conditions similar to in vivo scenarios seen in clinical practice. Needle placement is confirmed with fluoroscopy, subsequently, every provider at our institution will administer a short- or long-acting local anesthetic after motor or sensory testing for patient comfort prior to the ablative procedure. Lesion size with the no-fluid state and injection of solely hypertonic saline solution was not tested during this experiment, as this is not seen in clinical practice. To simulate in vivo scenarios, we used lidocaine in a 1:1 ratio with normal saline solution and hypertonic saline solution to standardize the volumes applied to the samples. The injectates administered (2% lidocaine, 0.9% saline solution, and 3% hypertonic saline solution) were chosen as those are commonly encountered in our clinical practice. Eight percent hypertonic saline solution used by other authors, such as Provenzano et al (7,8), were not used in our study as it is not readily available at our institution. Although this could be considered a potential limitation of our study, we feel that our parameters more closely simulate current clinical practice. Eighty degrees Celsius was chosen as our temperature parameter as per the American Society of Anesthesiologists clinical practice guidelines (15). Destruction of tissue occurs with probe temperatures between 60°C and 80°C (16). Coagulation starts on the surface at 65°C and as the temperature increases to 80°C, the volume of coagulation tissue increases (17). Clinically, a higher temperature

the ability to increase lesion size with the administration of hypertonic saline solution (15). Ablation of complex and large tumor geometries were simulated in ex vivo tissue of porcine liver and chicken breast (16). It is believed that increasing the sodium chloride concentration results in decreased impedance and increases the power measured by watts, thus improving conductance (7).

In this study, we attempted to demonstrate increased lesion size with increasing sodium chloride concentrations of the injectate. Comparatively of the 3 groups, 3% hypertonic saline solution and 2% lidocaine to a 1:1 ratio, and 0.9% normal saline solution and 2% lidocaine to a 1:1 ratio did not achieve a statistically significant larger burn size ac-

allows for larger lesion size, but raising the temperature above 90°C does not increase the size further (18-19). Additionally, temperatures above 80°C to 90°C can cause tissue gas formation and this can cause the patient harm, therefore 80°C was the optimal temperature for the ablation (12). At a lesion duration of 30 seconds, the lesion is 85% of the maximum lesion size, and at 60 seconds of energy delivery the lesion size is 94% of maximum lesion size (17). Generation of RF lesions using the Pain Management Generator (PMG, Baylis Medical Company, Montreal, Canada) indicated that it takes 15 seconds for the temperature of the cannula to reach 80°C, and an additional 60 seconds to produce the lesion (19). Thus the optimum lesion duration is more than 60 seconds, and therefore 90 seconds was chosen for the duration of ablation. Ninety seconds appears to be a standard across many studies conducted involving RF ablation (13,14).

The natural limitation of this ex vivo study is the fact that human organisms were not used, and therefore differences in tissue density could not be accounted for. Additionally, other physiological processes, including regulation of stable body temperature, could not be simulated. Inferences are drawn from poultry and porcine experiments to make conclusions on how human muscle and nervous tissue will behave to experimental variables. Human error is another limitation of this study, as inconsistent cuts and measurements of the study may occur. We accounted for this by having the same measurer for the entire experiment. Measures were taken to remain consistent by cutting the specimen over the RF probe and measuring at the widest radius across depth, longitudinal, and transverse measurements. Ellipsoid calculations cannot be inferred from a

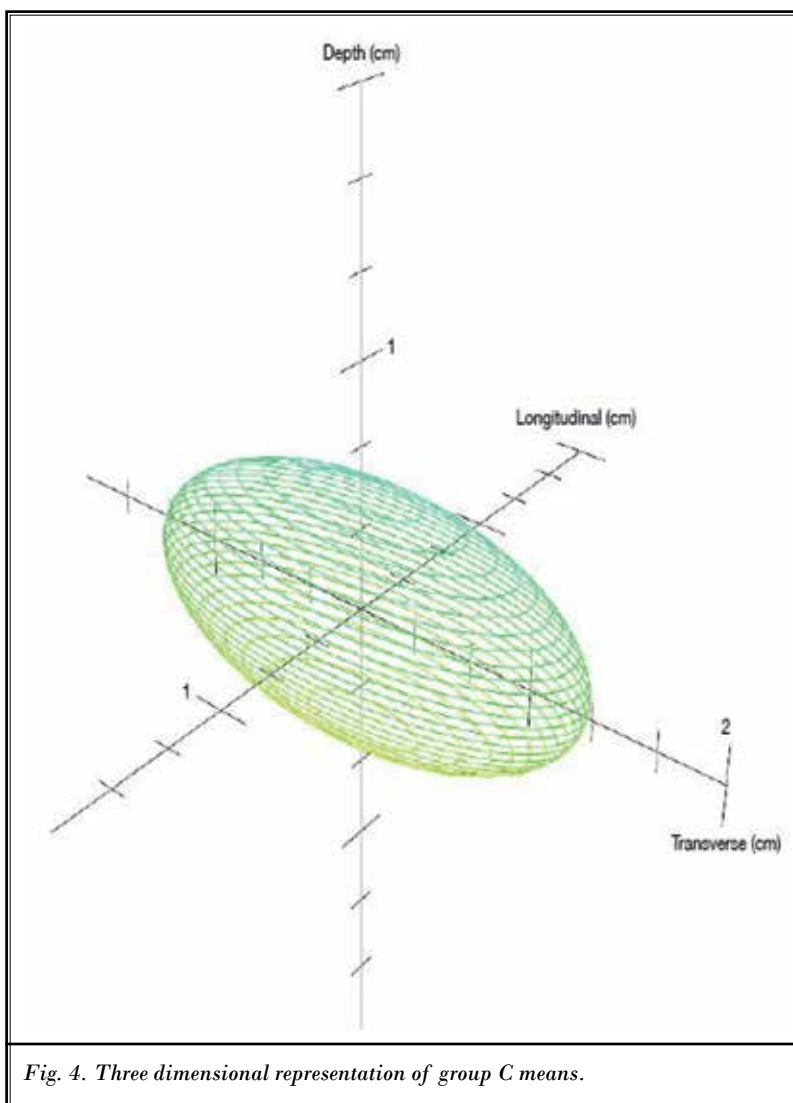


Fig. 4. Three dimensional representation of group C means.

2-dimensional measurement, thus the only way to achieve accuracy was to measure the maximal width in 3 dimensions.

Multiple studies, including several by Provenzano et al (7,8), display the effect of various fluids of different tonicities and the injection of fixed volumes on lesion size. Although our study was not the first ex vivo study performed on poultry, to our knowledge, it was the first double-blinded randomized control trial performed simulating in vivo scenarios. Our study reduces the experiment variables to 3 groups, resulting in improved sample size and increased power. This experiment also takes advantage of the central limit theorem. With the use of the Bonferroni correction, fewer groups lead to improved correction of type 1 error rate without reducing type 2 error rate.

CONCLUSIONS

In a randomized, double-blinded study, we were unable to show a difference between the 3 injectate groups. When RF ablation of the medial branch nerve of the dorsal rami is performed, priming the injectate with hypertonic saline solution does not result in a significantly increased lesion size. There was no benefit to

increasing the salinity of the solution, in fact, this may be more time-consuming and costly to the provider. Although it is known that the gauge size of the RFA needle, power and duration of the energy applied will confer changes to lesion size, injection of various concentrations of sodium chloride cannot be clinically applied based on this ex vivo study.

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