Radiofrequency induced lesion characteristics according to force–time integral in experimental model

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Abstract
Contact force (CF)-sensing technology has enabled accurate real-time CF measurement in tissue. Average CF, which is quantified by the force–time integral (FTI), correlates with lesion volume.

Little is known about which of the time and force factors that compose FTI plays a more important role and which is a better index for predicting lesion size, FTI, or force–power–time index (FPTI). Investigators sought to identify a better index for predicting radiofrequency ablation lesion formation with experimental model.

Radiofrequency current was delivered to the swine skeletal muscle at radiofrequency energy current was delivered at 4 fixed power settings (15, 25, 30, and 40 W) for 6 variable time durations (5, 10, 20, 30, 40, and 50 s) with 6 variable CF settings (5, 10, 20, 30, 40, and 50 g). At each setting, the following parameters were evaluated:

1. transmural lesion depth,
2. lesion width, and
3. lesion volume.

Between FTI factors, the time factor was more important than the force factor for lesion formation. The area under the curve was greater for FPTI (0.943) than for FTI (0.870). On univariate linear regression analysis, the explanatory power of the linear regression model was better explained by FPTI (56.4%) than FTI (32.1%).

Under the same FTI condition, the time factor had a greater effect on lesion formation. When power was included, the power factor had a greater effect on lesion formation and steam pop.

Abbreviations: AF = atrial fibrillation, CF = contact force, FTI = force (grams)–time (seconds) integral, HPSD = high-power short-duration radiofrequency ablation, RF = radiofrequency energy, RFCA = radiofrequency catheter ablation.

Keywords: cardiac electrophysiology, catheter ablation, radiofrequency ablation

1. Introduction
Radiofrequency catheter ablation (RFCA) is a treatment option for any cardiac arrhythmia. Despite the acute success of RFCA of arrhythmogenic foci, recurrences of arrhythmias after ablation are common, especially in atrial fibrillation (AF) and ventricular arrhythmia.[3] The recurrence rate of AF after a single procedure has been reported to be 15% to 60% after 1 year.[5] Recurrences are usually due to pulmonary vein reconnection in AF and inadequately ablated ventricular arrhythmia substrate.[6] This inability to achieve durable lesions remains one of the greatest challenges in RFCA for arrhythmias.

Lesion formation using radiofrequency energy (RF), current depends on several parameters such as power, contact force (CF) between the catheter tip and tissue, duration of energy delivery, temperature, tip size, and tip orientation.[6] Several studies reported that CF was a key factor to effective lesion formation.[7,8] A novel technology has recently been available to measure the CF between the catheter tip and the target myocardium using a unique sensor.[9] To characterize the effect of CF applied over time, the Carto 3 System ( Biosense Webster Inc., CA, USA) automatically detects the beginning and end of RF current delivery and calculates the force (grams)–time (seconds) integral (FTI; unit, g·s), defined as the total CF integrated over the duration of RF current delivery.[18] FTI consists of two factors: CF
and duration of energy delivery. Furthermore, some investigators have been developing the force (grams)–power (watts)–time (seconds) index (FPTI; unit, g·W·s), which considers the delivered energy, and attempting to apply it to clinical practice. This study is a qualitative study, aimed to investigate which factor is more critical for adequate lesion formation between CF and duration of energy delivery and which is more efficient for FTI and FPTI to predict lesion formation and steam pop.

2. Materials and methods

2.1. Force-sensing catheter

A 7.5 Fr open-irrigated tip catheter capable of CF-sensing technology, ThermoCool SmartTouch catheter (Biosense Webster Inc., CA), with a 3.5 mm catheter-tip electrode was used for this experiment. Three location sensors mounted on the shaft were capable of accurate (a resolution of 1 g every 50 ms) and real-time CF measurement. Force–time–integral (FTI = unit, g·s) is defined as the total CF integrated over the duration of RF current delivery, while FPTI is additional index considering delivered energy (FPTI = unit, g·W·s).

2.2. Experimental preparation

Swine skeletal muscle (loin) was obtained from a butcher shop. A motor drive moving platform was created for an in vitro model simulating the beating heart. A ThermoCool SmartTouch catheter (Biosense Webster Inc., CA, USA) was placed on the tissue specimen over a vibrating platform placed within a tank filled with physiologic saline solution at 36.5°C (Fig. 1). The platform was continuously vibrated at a rate of 50 cycles per minute by an electronic motor. An RF generator (Stockert GmbH, Freiburg, Germany) was connected to deliver an RF current of 550kHz between the catheter-tip electrode and a ground plate in the tank. A calibrated roller pump (CoolFlow irrigation pump, Biosense Webster Inc., CA, USA) connected to the irrigation port of the catheter delivered normal saline solution at a rate of 17 mL/min for ablation power below 30 W and 30 mL/min for ablation power above 30 W. The CARTO 3 system (Biosense Webster Inc., CA) used for the CF data is fully integrated into the system display and can be configured to show the data at several locations on the screen.

2.3. Experimental protocol

RF current was delivered at 4 fixed power settings (15, 25, 30, and 40 W) for 6 variable time durations (5, 10, 20, 30, 40, and 50 s) with 6 variable CF settings (5, 10, 20, 30, 40, and 50 g). At each setting, the following parameters were evaluated:

1) transmural lesion depth,
2) lesion width, and
3) lesion volume.

To minimize the effect of heterogeneous individual tissue characteristics, ablations were repeated at least 5 times for each set of experimental conditions. The dimensions of the blanched lesion zone were measured using a digital caliper with a resolution of 0.01 mm by an observer who was blinded to the ablation protocol. The lesion width (w) and lesion depth (d) in sectioning are shown in Figure 2. Lesion volumes were calculated using the following formula for a half ellipsoid: \( 2/3 \times \pi \times d \times (w \times w/4) \). The incidence of steam pop (the audible sudden build-up of steam) was also recorded. This study was approved by the Institutional Ethics Committee and Review Board at Asan Medical Center.

2.4. Statistical analysis

Statistical analysis was performed using SPSS for Windows version 21.0 (IBM Corporation, Armonk, NY). A P-value of <.05 was considered to indicate statistical significance. Univariate linear regression analysis was performed to assess the individual effects on lesion formation and steam pop, whereas multiple linear regression analysis was used to explain the relationship between dependent and independent variables. It was believed that there was a problem of multicollinearity when the variance inflation factor exceeded 10. The Durbin–Watson statistic was used to detect the presence of autocorrelation (a relationship between values separated from each other by a given time lag) in the residuals (prediction errors). A receiver operating characteristic curve was used to determine the threshold for steam pop.

3. Results

3.1. Differences in the effect of force and time factors on lesion formation in the same force–time integral value

A total of 336 lesions were created according to the experimental protocol. There were differences in the effect of force and time factors on lesion depth, diameter, and volume under the same FTI condition at each power. In particular, between FTI factors, the time factor was 1.6 to 2.9 times more important than the force factor for lesion formation. In cases with steam pop, the effect of force was greater than that of time (Table 1A and B).
3.2. FTI and FPTI values to predict steam pop

The best discriminating cut-off values for steam pop with the highest sensitivity and specificity were 700 g·s (sensitivity = 83.3%, specificity = 74.2%, positive predictive value 46.9%, and negative predictive value 94.2%) for FTI and 31,000 g·W·s (sensitivity = 80.6%, specificity = 97.7%, positive predictive value 80.6%, and negative predictive value 94.7%) for FPTI. The area under the curve for FPTI (0.943) was greater than that for FTI (0.870) (Fig. 3).

Table 1

(A) Effect of force and time factors on lesion depth, diameter, and volume at an FTI value of 500 g·s at each power, (B) Variations in depth, diameter, volume, and steam pop according to changes in force and time at each power.

| Energy (W) | Force (g) | Time (s) | FTI (g·s) | Depth (mm) | Diameter (mm) | Volume (mm³) | Steam pop |
|-----------|-----------|----------|-----------|------------|---------------|--------------|-----------|
| 15        | 50        | 10       | 500       | 3.15       | 5.11          | 43.05        | No        |
| 15        | 10        | 50       | 500       | 4.75       | 5.45          | 73.84        | No        |
| 25        | 50        | 10       | 500       | 5.56       | 6.20          | 91.53        | No        |
| 25        | 10        | 50       | 500       | 6.82       | 6.55          | 143.92       | No        |
| 30        | 50        | 10       | 500       | 4.70       | 5.66          | 80.31        | No        |
| 30        | 10        | 50       | 500       | 6.98       | 6.42          | 150.56       | No        |
| 40        | 50        | 10       | 500       | 4.50       | 8.15          | 156.42       | Yes       |
| 40        | 10        | 50       | 500       | 6.25       | 10.45         | 357.18       | Yes       |

| Power (W) | Depth (Δ, %) | Diameter (Δ, %) | Volume (Δ, %) | Steam pop (Δ, %) |
|-----------|--------------|-----------------|---------------|-----------------|
| 15        | 32.9°*       | 23.3°**         | 37.8°         | N/A             |
| 25        | 31.8°        | 47.3°           | 46.8°         | 47.8°           |
| 30        | 34.1°        | 43.4°           | 45.6°         | 53.6°           |
| 40        | 25.5°**      | 31.2°           | 27.2°         | 61.1°           |

FTI = force-time integral.
* P < .01.
** P < .05.
3.3. Effect of power, force, and time at an FTI value below 700 g·s and FPTI value below 31,000 gW

There was similarity to the overall results at an FTI value below 700 g·s and FPTI value below 31,000 gW. With respect to lesion formation, time was a more important factor than force. In cases with steam pop, force was a more important factor than time (Table 2).

3.4. FTI vs. FPTI: a more accurate method to predict lesion formation (Fig. 4, Table 3)

Univariate linear regression analysis was performed to examine the predictability of FTI and FPTI for lesion formation and steam pop. In the case of FPTI, an explanatory power of 56.4% and 32.7% was shown for lesion formation and steam pop, respectively. In the case of FTI, an explanatory power of 53.9% was shown for lesion formation and steam pop, which could be represented by complications. Moreover, under the same FTI condition, the lesion formed (lesion volume) increased by 73.6% to 83.6% with increasing time, but the lesion increased by only 27.2% to 46.8% with increasing force. This result can be explained by the following coexisting mechanisms:

1. rapid resistive heating of the thin rim of the tissue surrounding the ablation electrode and
2. conductive heating of the deep tissue, which occurs much more slowly.[6,12,13]

It is considered that sufficient time is required to achieve the thermal equilibrium for slow subsequent conductive heating. The ThermoCool SmartTouch catheter (Biosense Webster Inc., CA) measures CF values (in grams) averaged on 500 ms time interval. Its ability to measure CF in real time at the tip of an ablation catheter can monitor the quality of catheter–tissue contact in a situation that is dependent on the operator’s experience in the pre-CF era. The zone of resistive heating extends only about 1 mm from the catheter-tip electrode, because energy delivery and heating are inversely proportional to the fourth power of distance from the catheter tip.[13] Therefore, high-quality catheter–tissue contact is important to cause necrosis in

4. Discussion

Creating a transmural lesion without causing complications is important for the interventional treatment of arrhythmias, but this needs precaution and several aspects need to be considered. Modern technology, such as CF-sensing technology, has improved the efficiency of RFCA. However, it is necessary to understand parameters such as FTI derived from this technique. This study assessed the effect of force and time factors that compose FTI on lesion formation and complication.

The main findings of the present study are as follows:

1. among the elements constituting FTI, the time factor has a greater effect on lesion formation than the force factor;
2. in cases with steam pop associated with complications, the force factor is more involved than the time factor;
3. taking the delivered power into account, the FPTI value is a better predictor of complication than the FTI value; and
4. the FPTI value is a more accurate predictor of lesion formation than the FTI value.

The present study confirmed the findings of a previous study[11] that both force and time were positively correlated with lesion formation and steam pop, which could be represented by complications. Moreover, under the same FTI condition, the lesion formed (lesion volume) increased by 73.6% to 83.6% with increasing time, but the lesion increased by only 27.2% to 46.8% with increasing force. This result can be explained by the following coexisting mechanisms:

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**Table 2**

| FTI value below 700 g·s | Power (Δ) | Force (Δ) | Time (Δ) | FPTI value below 31,000 gW·s | Power (Δ) | Force (Δ) | Time (Δ) |
|------------------------|-----------|-----------|----------|-----------------------------|-----------|-----------|----------|
| Depth (Δ, %)           | 46.1*     | 30.3*     | 79.2*    | Diameter (Δ, %)             | 60.9*     | 37.6*     | 59.6*    |
|                        | 65.7*     | 23.4*     | 63.2*    | Volume (Δ, %)               | 27.1*     | 25.9*     | 66.1*    |
|                        | 34.3*     | 32.2*     | 23.8*    | Steam pop (Δ, %)            | 13.3      |

FPTI=force–power–time index, FTI=force–time integral.

* P < .05.
** P < .01.
the targeted tissue. However, under experimental condition in which continuous contact is assured, the time factor is believed to be more important than the force factor for lesion formation.

The force factor had a greater effect on steam pop than the time factor at a high-energy setting (53.6% vs. 28.7% at 30 W and 61.1% vs. 47.2% at 40 W, respectively). When the tissue temperature exceeds 100°C, the boiling of water in the myocardial tissue can cause a sudden steam build-up, sometimes audible as a steam pop. When the catheter tip is located in an area with poor convective blood cooling, such as in a pouch or between tissue trabeculations, the catheter-tip electrode can be excessively heated. Under this experimental condition, a high CF artificially leads to this situation. The high CF in the soft tissue results in the catheter tip being buried in the tissue. As steam pop may be associated with cardiac rupture or tamponade, it is conceivable that it is better clinically to not make the CF too high in relatively soft tissues.

Recently, high-power short-duration radiofrequency ablation (HPSD) is studied and showed efficacy and safety compared to previous conventional ablation technique. Usually conventional ablation technique with standard power (25–30 W), to create durable ablation lesion, catheter stability for longer time is essential. With standard technique, conductive heating is the main component of lesion formation, while with HPSD technique, resistive heating is. Lesion depth and width increased with higher power, and that is proven in our technique, resistive heating is. Lesion depth and width the main component of lesion formation, while with HPSD time is essential. With standard technique, conductive heating is to create durable ablation lesion, catheter stability for longer conventional ablation technique with standard power (25 W), it is considered that a parameter such as FPTI that considers power in the FTI value is better as a single surrogate marker than FTI. More research is required to develop a marker that can better explain lesion formation than FPTI, which is a relatively simple index. Recently, the Ablation index, which is a complex weighted exponential formula assigning different weights to power, CF, and time (power receiving a higher weighting than CF), has been experimentally and clinically studied. Ablation index is similar to FPTI in terms of reflecting power, CF, and time but Ablation index is calculated as a weighted formula of power, CF, and time. In this in vitro experimental model, we used FPTI for intuitive estimation of lesion formation.

When analysed only under FTI 700 and FPTI 31000, in which steam pop did not appear, it was found that the time factor was involved in lesion formation and the force factor was more involved in the formation of the steam pop. When power was included and analysed, the power factor had a greater effect on lesion formation and steam pop than other factors. This suggests again that FPTI, which considers power, is a better indicator than the power-free FTI. This gives clinical implication during applying HPSD technique, which ablation lesion is larger and steam pop occur more frequently. We suggest distance between

| Table 3 |
| Associations of lesion formation and steam pop with FTI and FPTI according to univariate linear regression analysis. |

| FTI on depth | FTI on diameter | FTI on volume | FTI on steam pop | FPTI on depth | FPTI on diameter | FPTI on volume | FPTI on steam pop |
|--------------|-----------------|---------------|------------------|---------------|------------------|---------------|------------------|
| 0.468        | 0.193           | 0.321         | 0.277            | 0.480         | 0.323            | 0.264         | 0.539            |
| 0.684        | 0.439           | 0.566         | 0.572            | 0.693         | 0.569            | 0.791         | 0.734            |
| <.01         | <.01            | <.01          | <.01             | <.01          | <.01             | <.01          | <.01             |

FTI=force–time index, FPTI=force–power–time index.
the ablation points should be farther in HPSD than standard power ablation technique.

5. Limitations
This study is subject to limitations inherent in an experimental study. Firstly, it may be difficult to apply this result to clinical practice because the experiment was performed on the relatively smooth skeletal muscle tissue rather than the heart tissue. In addition, even though the cardiac contractile model was used to simulate real cardiac movement, it is not identical to that of beating heart. Secondly, the experimental study was performed in a more refined environment than in clinical practice. During the experiment, catheter orientation maintained only vertically, to maintain constant CF, which does not reflect changes in catheter orientation (i.e. angle of catheter contact) and CF related to heartbeat or respiration during the actual ablation procedure. Thirdly, because we used power, time, and CF derived from experiments performed on the cardiac tissue, the results can be overestimated or underestimated.

6. Conclusion
Under the same FTI condition, the time factor had a greater effect on lesion formation than the force factor. Time was believed to be a more important factor than CF under the same FTI condition to create an adequate RF ablation lesion. When power was included and analysed, the power factor had a greater effect on lesion formation and steam pop than other factors as we demonstrated in this experimental model. Since, FTI does not take the power used during RF application into account, FPTI is useful and safe parameter to estimate ablation lesion depth and quality during RF ablation.

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