Comparison of Wet Radiofrequency Ablation with Dry Radiofrequency Ablation and Radiofrequency Ablation Using Hypertonic Saline Preinjection: Ex Vivo Bovine Liver

Objective: We wished to compare the in-vitro efficiency of wet radiofrequency (RF) ablation with the efficiency of dry RF ablation and RF ablation with preinjection of NaCl solutions using excised bovine liver.

Materials and Methods: Radiofrequency was applied to excised bovine livers in a monopolar mode for 10 minutes using a 200 W generator and a perfused-cooled electrode with or without injection or slow infusion of NaCl solutions. After placing the perfused-cooled electrode in the explanted liver, 50 ablation zones were created with five different regimens: group A; standard dry RF ablation, group B; RF ablation with 11 mL of 5% NaCl solution preinjection, group C; RF ablation with infusion of 11 mL of 5% NaCl solution at a rate of 1 mL/min, group D; RFA with 6 mL of 36% NaCl solution preinjection, group E; RF ablation with infusion of 6 mL of 36% NaCl solution at a rate of 0.5 mL/min. In groups C and E, infusion of the NaCl solutions was started 1 min before RF ablation and then maintained during RF ablation (wet RF ablation). During RF ablation, we measured the tissue temperature at 15 mm from the electrode. The dimensions of the ablation zones and changes in impedance, current and liver temperature during RF ablation were then compared between the groups.

Results: With injection or infusion of NaCl solutions, the mean initial tissue impedance prior to RF ablation was significantly less in groups B, C, D, and E (43 \pm 75 \Omega) than for group A (80 \Omega) (p < 0.05). During RF ablation, the tissue impedance was well controlled in groups C and E, but it was often rapidly increased to more than 200 \Omega in groups A and B. In group D, the impedance was well controlled in six of ten trials but it was increased in four trials (40\%) 7 min after starting RF ablation. As consequences, the mean current was higher for groups C, D, and E than for the other groups: 401 \pm 145 mA in group A, 287 \pm 32 mA in group B, 1907 \pm 96 mA in group C, 1649 \pm 514 mA in group D, and 1968 \pm 108 mA in group E (p < 0.05). In addition, the volumes of RF-induced coagulation necrosis were greater in groups C and E than in group D, which was greater than in groups A and B than in group E (p < 0.05): 14.3 \pm 3.0 cm³ in group A; 12.4 \pm 3.8 cm³ in group B; 80.9 \pm 9.9 cm³ in group C; 45.3 \pm 11.3 cm³ in group D and 81.6 \pm 8.6 cm³ in group E. The tissue temperature measured at 15 mm from the electrode was higher in groups C, D and E than other groups (p < 0.05): 53 \pm 12 °C in group A, 42 \pm 2 °C in group B, 93 \pm 8 °C in group C; 79 \pm 12 °C in group D and 83 \pm 8 °C in group E.

Conclusion: Wet RF ablation with 5% or 36% NaCl solutions shows better efficiency in creating a large ablation zone than does dry RF ablation or RF ablation with preinjection of NaCl solutions.
Image-guided percutaneous radiofrequency (RF) ablation has become increasingly popular in recent years, and it has been accepted as an alternative to surgical resection for the treatment of primary and secondary hepatic malignancy in inoperable patients (1–4). However, current RF technology is limited in that only tissue 3.5 to 4.5 cm in diameter could be ablated with a single application of RF energy (5–9). This inherent limitation of monopolar RF ablation, in regards to the small dimension of coagulation necrosis, is attributed to resistive heating at a narrow rim of tissue that surrounds the electrode (1, 2, 10). There is always a rapid increase of temperature at the tissue-electrode interface, and this results in tissue desiccation and charring at the electrode tip. These effects prevent further RF energy conduction beyond the desiccated tissue and this halts further tissue coagulation.

There have been several reported strategies to solve this limitation of monopolar RF ablation including RF ablation with hypertonic saline (HS) preinjection (11–13), wet RF ablation (RF ablation with continuous infusion of HS through the electrode) (14–16), bipolar RF ablation (17, 18), and RF ablation using multiple probes (19–21). Among these approaches, we believe that hypertonic saline-mediated RF ablation, which includes RF ablation with HS preinjection and wet RF ablation, is seemingly a very attractive method because the injected saline could increase both the electrical and thermal conductivities, and the higher boiling points of the hypertonic saline could be helpful in avoiding the rapid boiling of liver tissue adjacent to the electrode (12, 20, 22, 23). Until now, however, there has been no well-designed comparative study between RF ablation with HS preinjection and wet RF ablation using HS infusion. In this context, we conducted a study to verify whether wet RF ablation has better efficiency in creating an ablation zone than does dry RF ablation or RF ablation with HS preinjection, and we did this by measuring the dimensions of the ablation zones in liver tissue, and by measuring the tissue temperature.

**MATERIALS AND METHODS**

**RF Ablation Settings**

Based on the previous studies that described consistent results for tissue ablation from ex vivo RF ablation experiments (16, 17, 24, 25), we chose to use excised beef liver purchased from a local butcher as the RF ablation target for our experiment. RF ablation was performed in 25 freshly excised bovine livers weighing, on average, 7.5 Kg each. The livers were cut into several 10 × 10 ×10-cm³ blocks that were dipped into a 50 ×20 ×20-cm³ saline-filled bath at room temperature.

The RF ablation system we used was composed of a 15-gauge perfused-cooled electrode with 3 cm tip exposure, and a 480 kHz generator (CC-3, Radionics, Burlington, Mass) was used at 200 watts. As described in a previous study (24), we developed a perfused-cooled electrode to permit both intra-electrode cooling perfusion and interstitial saline infusion. We modified a 17-gauge cooled-tip electrode with a 3-cm active tip (Radionics) by covering it with a 15-gauge outer sheath, which was made of metal and electrically insulated, except for the 3.5 cm distal portion (Fig. 1).

The 15-gauge perfused-cooled electrode was advanced at least 4 cm into the target liver tissue. To continuously measure the local tissue temperature during the procedure, a thermocouple was inserted at 15 mm from the electrode. Tissue impedance was monitored using the circuitry incorporated into the generator. A peristaltic pump (Watson-Marlow, Medford, Mass) was used to infuse 0 °C saline solution into the lumen of the electrodes at a rate sufficient to maintain the tip temperature at 20–25 °C. The 5% or 36% NaCl solutions were infused through a perfused-cooled electrode using an infusion pump (Pilotec IS; Fresenius Medical Care, Alzenau, Germany). The applied current, power output, and impedance were continuously monitored during the RF ablation, and these parameters were recorded automatically using a computer program (Real Time Graphics Software V 2.0; Radionics).

**Ablation Protocol**

Radiofrequency was applied to the excised bovine livers in monopolar mode for 10 minutes using a 200 W generator (Radionics) and a perfused-cooled electrode. To compare the performance of the wet RF ablation with dry RF ablation and RF ablation with HS preinjection for creating coagulation necrosis, 50 ablation zones were

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**Fig. 1.** Photograph of the perfused-cooled electrode which was used for wet RF ablation.
created at five different regimens: group A; standard dry RF ablation, group B; RF ablation with 11 cc of 5% NaCl solution preinjected, group C; wet RF ablation with infusion of 11 cc of 5% NaCl solution at a rate of 1 mL/min, group D; RF ablation with 6 cc of 36% NaCl solution preinjected, and group E; wet RF ablation with infusion of 6 cc of 36% NaCl solution at a rate of 0.5 mL/min. In groups C and E, infusions of NaCl solutions were started before RF ablation (1 mL) and this was maintained during RF ablation at predetermined infusion rates (wet RF ablation). The initial impedance was set at 80 ohm with the electrode insertion by altering the distance between the electrodes and the dispersive metallic pad. Based on previous studies regarding saline-mediated RF ablation, 5% and 36% NaCl solutions were selected as the test solutions (12, 22, 26). Based on the results of the previous study regarding the optimal concentration and volume of NaCl for RF ablation (12), a volume of 6 mL saturated HS (36% NaCl) was used for comparison between the two RF ablation techniques. To create the same condition between the wet-RF ablation and the RF ablation with preinjection of NaCl solutions, in group E (wet RF ablation), 1 mL of 36% NaCl was infused prior to the RF ablation and 5 mL of the solution were injected during the RF ablation at a rate of 0.5 mL/min. Furthermore, based on other previous studies regarding wet RF ablation (17, 26), 5% NaCl at a rate of 1 mL/min was selected to be infused. To create the same condition between the two techniques, a volume of 11 mL was selected to be preinjected.

The technical aspects of the RF ablation including impedance and wattage changes, tissue temperature measured at 15 mm from the electrode, and the dimensions of the RF-coagulated area were compared for each condition.

Lesion Size Measurement
Liver blocks containing the RF ablation lesions were dissected along the longitudinal plane passing through the axes of the probe (the L-plane), and then we cut the blocks transversely and perpendicular to the L-plane (the T-plane). As the white central area of the RF induced ablation zone has been previously shown to correspond with the zone of coagulation necrosis (27, 28), two observers measured the vertical diameter (DV) along the probe, and the transverse diameter (DT1) perpendicular to the DV in the L-plane, and the second transverse diameter of the ablation zone (DT2) in the T-plane (Fig. 2). The volumes of ablation zones were evaluated by approximating the lesion to a sphere using: \( \pi(DV \times DT1 \times DT2)/6 \).

The shape of the RF-induced ablation zone was assessed by means of the DT1/DV ration.

Statistical Analysis
The dimensions of the thermal ablation area and the technical parameters of the five groups were averaged for each group, and these were compared using a one-way analysis of variance (ANOVA) test. For the comparison between the groups, Bonferroni multiple comparison test was used. Values were expressed as means ± standard deviation. To compare the tissue temperature at 15 mm from the electrode tips, repeated measures of ANOVA test were performed. For all the statistical analyses, a \( p \) value of less than 0.05 was considered significant. Statistics were performed using the Instat program (GraphPad Software, Inc., San Diego, Cal).

RESULTS

Electrical Measurements
The mean initial tissue impedance prior to the RF ablation was significantly lower in the groups with injection or infusion of NaCl solutions (43–75 Q) than group A (80 Q) (Table 1) (\( p < 0.05 \)). In addition, during the RF ablation, the tissue impedance was well controlled.
in groups C and E, but it was often rapidly increased to more than 200 Ω in groups A and B (Fig. 3). In group D, the impedance was well controlled in six of ten trials, but it was increased in four (40%) trials 7 min after starting the RF ablation. As a consequence, the mean current was higher for groups C, D, and E than for the other groups: 401 ± 145 mA in group A, 287 ± 32 mA in group B, 1907 ± 96 mA in group C, 1649 ± 514 mA in group D, and 1968 ± 108 mA in group E (p < 0.05).

**Temperature**

The graphs showing the mean temperature at 15 mm from the electrode tips are shown in Fig. 4. The mean final midpoint temperature values were 53 ± 12 °C in group A, 42 ± 2 °C in group B, 93 ± 8 °C in group C, 79 ± 12 °C in group D and 83 ± 8 °C in group E. The tissue temperatures were higher in groups C, D, and E than in groups A and B (p < 0.05).

Table 1. Measured Values of Electrical Parameters Related to Radiofrequency Ablation for the Five Groups

| Parameter                                      | Group A | Group B | Group C | Group D | Group E | p Value |
|------------------------------------------------|---------|---------|---------|---------|---------|---------|
| Initial Tissue Impedance before infusion       | 80      | 80      | 80      | 80      | 80      | p > 0.05 |
| or injection of NaCl solutions (ohm)           |         |         |         |         |         |         |
| Initial Tissue Impedance after infusion        | 59 ± 3.4| 75 ± 1.1| 43 ± 2.3| 71 ± 1  |         | p < 0.05* |
| or injection of NaCl solutions (ohm)           |         |         |         |         |         |         |
| Mean Impedance during RFA (ohm)                | 311 ± 62| 339.8 ± 30| 57.3 ± 3| 111.4 ± 94| 51.82 ± 2| p < 0.05† |
| Mean Current during RFA (mA)                   | 401 ± 145| 287 ± 32| 1907 ± 96| 1649 ± 514| 1968 ± 108| p < 0.05* |

Note.—RFA = radiofrequency ablation. Group A = dry RFA, group B = RFA with hypertonic saline preinjection (5%), group C = wet-RFA (5%), group D = RFA with hypertonic saline preinjection (36%), group E = wet-RFA (36%). * There were significant differences between dry RFA and other groups, †There were significant differences between groups C, D and E, and groups A and B.
Dimensions of the Zones of Ablation

After RF ablation, a well-defined area with a central white discoloration was observed in the ablated zone sections. The mean DVs of the RF induced central white zones on the L-plane measured in the gross specimens for each group were larger for groups C, D, and E than for groups A and B: 4.9 ± 0.7 cm in group A, 4.4 ± 0.5 cm in group B, 6.1 ± 0.5 cm in group C, 4.9 ± 0.4 cm in group D and 6.0 ± 0.5 cm in group E (p < 0.05) (Table 2). In addition, the DT1s on the L plane were as follows: 2.4 ± 0.3 cm in group A, 2.4 ± 0.3 in group B, 5.1 ± 0.4 in group C, 4.3 ± 1.5 cm in group D, and 5.1 ± 0.3 cm in group E. The DT1s of the RF-induced coagulation necrosis were greater in groups C and E than in group D, which was greater than in groups A and B (p < 0.05) (Fig. 5). In addition, the mean DT2 of the ablated spheres were also larger in groups C, D, and E than in groups A and B: 2.4 ± 0.3 cm in group A; 2.2 ± 0.3 cm in group B; 5.2 ± 0.6 cm in group C, 4.2 ± 0.5 cm in group D and 5.4 ± 0.4 cm in group E, respectively (p < 0.05).

The volumes of RF-induced coagulation necrosis were greater in groups C and E than in group D, which was greater than in groups A and B (p < 0.05): 14.3 ± 3.0 cm³ in group A, 12.4 ± 3.8 cm³ in group B, 80.9 ± 9.9 cm³ in group C, 45.3 ± 11.3 cm³ in group D, and 81.6 ± 8.6 cm³ in group E. Furthermore, the ratio of DT1/DV were 0.6 ± 0.1 in group A, 0.6 ± 0.1 in group B, 0.9 ± 0.1 in group C, 0.9 ± 0.1 in group D and 0.9 ± 0.1 in group E. The ratio of DT1/DV in groups A and B were significantly less than those of groups C, D, and E (p < 0.05). This means that the groups C, D, and E tended to produce a more spherically-shaped coagulation than the other groups (groups A and B).

DISCUSSION

The limitation of the current monopolar RF ablation system is related to the fact that the current density drops off at rate proportional to the inverse square of the distance from the electrode. Therefore, heating preferentially takes places immediately adjacent to the electrode, leading to rapid charring and a decrease of current delivery (1, 2, 20). One of the most effective approaches to overcome this problem is to infuse NaCl solution into target tissue, and this increases both the electrical conductivity and thermal conductivity (12, 22, 23). Two ways have been reported for using NaCl solution to increase the efficacy of monopolar RF ablation for creating coagulation necrosis: one is bolus injection of NaCl solution prior to RF ablation and the other way is a continuous infusion of NaCl solution prior to and during the RF ablation. Although several studies have demonstrated that both methods were useful to enlarge the ablation area as compared to the standard dry RF ablation (11–16, 22, 23, 29–31), it would be useful to determine which technique can efficiently induce a larger ablation area.

Our results show that the wet RF ablation with 5% or 36% NaCl solutions or RF ablation with preinjection of 36% NaCl solution created larger ablation zones than did the dry RF ablation (p < 0.05): 14.3 ± 3.0 cm³ in group A, 80.9 ± 9.9 cm³ in group C, 45.3 ± 11.3 cm³ in group D and

![Fig. 4. Graphs of mean tissue temperatures at 15 mm from the electrode in each group. Note that a higher temperature was achieved in groups C, D, and E than in groups A and B.](image)

Table 2. Measured Values of Diameters and Volumes of Radiofrequency-Induced Coagulation and Tissue Temperatures in the Five Groups

| Coagulation Necrosis | Group A | Group B | Group C | Group D | Group E | p Value |
|----------------------|---------|---------|---------|---------|---------|---------|
| DV (cm)              | 4.9 ± 0.7 | 4.4 ± 0.5 | 6.1 ± 0.5 | 4.9 ± 0.4 | 6.0 ± 0.5 | p < 0.05* |
| DT1 (cm)             | 2.4 ± 0.3 | 2.4 ± 0.3 | 5.1 ± 0.4 | 4.3 ± 1.5 | 5.1 ± 0.3 | p < 0.05† |
| DT2 (cm)             | 2.4 ± 0.3 | 2.2 ± 0.3 | 5.2 ± 0.6 | 4.2 ± 0.5 | 5.4 ± 0.4 | p < 0.05* |
| Volume (cm³)         | 14.3 ± 3.0 | 12.4 ± 3.8 | 80.9 ± 9.9 | 45.3 ± 11.3 | 81.6 ± 8.6 | p < 0.05† |
| Ratio of DT1/DV      | 0.6 ± 0.1 | 0.6 ± 0.1 | 0.9 ± 0.1 | 0.9 ± 0.1 | 0.9 ± 0.1 | p < 0.05* |
| Temperature (°C)*    | 53 ± 12 | 42 ± 2 | 93 ± 8 | 79 ± 12 | 83 ± 8 | p < 0.05* |

Note. — Group A = dry radiofrequency ablation (RFA), group B = RFA with hypertonic saline (HS) preinjection (5%), group C = wet-RFA (5%), group D = RFA with HS preinjection (36%), group E = wet-RFA (36%), DV = vertical diameter, DT1 = transverse diameter on the plane along the electrode, DT2 = transverse diameter on the transverse plane.

* There were significant differences between groups C, D, and E, and groups A and B. † The values in groups C and E were greater than in group D, which was greater than in groups A and B.
81.6 ± 8.6 cm³ in group E. These differences are probably related to the delivery of a higher current throughout the procedure, and this was attributed to the constant low impedance below 100 Ω. Regardless of the delivery methods of the NaCl solutions to the target tissue, the NaCl solutions increase the electrical conductivity and increase the current delivery from the electrode to the tissue (11, 12) (Table 1).

More importantly, the wet RF ablation with 5% or 36% NaCl solutions created larger ablation zones than did RF ablation with a preinjection of 5% or 36% NaCl solutions. The better performance of wet-RFA compared to RF ablation with a preinjection of hypertonic saline could be attributed to several factors. First, in wet RF ablation using the perfused-cooled electrode, some of the infused saline could diffuse out from the electrode, but the diffusing saline is continuously replaced by a slow infusion (25). However, in RF ablation with a preinjection of NaCl solutions, the injected solution could rapidly diffuse out depending upon the tissue pressure. Furthermore, for the in vivo situation, infused saline could be washed-out by perfusion. The less proportion of injected saline that remains in situ, the less enhancement of RF ablation efficacy is expected. Therefore, theoretically at least, wet RF ablation may have the effect to enhance RF ablation efficacy by increasing electrical and thermal conductance in a more stable and predictable way than the pre-RF ablation injection of NaCl solution. Second, for the wet RF ablation, the infused liquid continuously fills the gap between the metal electrode and the adjacent tissue, and this pushes the electrically insulating gases away from the electrode (30). This phenomenon can probably not be expected to happen for RF ablation with a preinjection of NaCl solution. Third, the infused liquid allows for some convective cooling at the tip of the electrode.

When considering the concentration of the injected NaCl solutions, RF ablation with a preinjection of 36% NaCl solution showed a better performance for creating a larger ablation necrosis zone than RF ablation that was done with a preinjection of 5% NaCl solution. This result could be attributed to the following factors. First, the higher ion concentration resulting from 36% NaCl solution could increase the electrical conductance of the tissue, and therefore, this may decrease too much concentration of the

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**Fig. 5.** Comparison of radiofrequency-induced ablation areas in the five groups. Arrow indicates the electrode insertion site and arrowhead indicates the thermocouple insertion site.

A. Photograph of specimen from group A (standard dry RF ablation).
B. Photograph of specimen from group B (RF ablation with 11 mL of 5% NaCl solution preinjection).
C. Photograph of specimen from group C (wet RF ablation with infusion of 11 mL of 5% NaCl solution).
D. Photograph of specimen from group D (RF ablation with 6 mL of 36% NaCl solution preinjection).
E. Photograph of specimen from group E (wet RF ablation with infusion of 6 mL of 36% NaCl solution).
electrical energy at tissue adjacent to the electrode and prevent boiling of the tissue. Second, because 36% NaCl has a higher boiling point than 5% NaCl, the charring of the tissue contains 36% NaCl solution could be prevented. Furthermore, we found that RF ablation with a preinjection of 5% NaCl produced a rather smaller ablation zone than the dry RF ablation, although the difference was not statistically significant ($p > 0.05$). This finding could be attributed to the increased production of electrically insulating gases compared to dry RF ablation; these gases fill the gap between the metal electrode and the tissue and increase the value of the impedance. Although the electrical conductivity of the tissue can be increased with an injection of 5% NaCl solution, the 5% saline solution may not be ionic enough to prevent too much concentration of the electrical energy in the tissues adjacent to the electrode.

However, for the wet RF ablation, both groups C and E did not show any difference in the volume of the coagulation necrosis. This suggests that the increased efficacy of wet RF ablation in creating coagulation necrosis is possibly due to both increased electrical conductance and increased hydration. Although the infusion of larger amounts of a lower concentration of NaCl induces less change in electrical conductance than the infusion of a smaller amount of higher concentration NaCl, it may induce a larger hydration effect than does the latter solution. Therefore, infusion of 5% NaCl solution at 1 mL/sec could allow for more gap filling between the metal electrode and the tissue and also it could create some convective cooling at the tip more than the infusion of 36% NaCl solution at 0.5 mL/sec. Furthermore, it could induce better thermal conductivity of the tissue than does an infusion of 36% NaCl solution at 0.5 mL/sec. Further study regarding the optimal concentration and volume of NaCl solution for wet RF ablation will be warranted to provide both the effects of increasing electrical conductance and hydration during RFA.

Although we did not test 36% NaCl at high infusion rates, we believe that decreasing tissue impedance too much would not be helpful to increase RF-induced coagulation necrosis because too large a decrease of tissue impedance induces a remarkable increase of current needed to create the heat (23). Furthermore, Ahmed et al. (32) have well demonstrated that the use of RF energy for tumors surrounded by poorly conductive tissues can result in increased heating at the margins of the ablation zone, and these researchers demonstrated this in a previous study regarding the effect of surrounding tissue composition on coagulation necrosis during RF ablation. Therefore, although an increasingly negative linear correlation was observed between the tumor coagulation diameter and the overall baseline system impedance, too great a decrease for the impedance of the surrounding tissue, as well as a decrease of tumoral impedance by the injected HS, could potentially hinder complete tumor destruction.

In our study, wet RF ablation and RF ablation with preinjection of NaCl solutions showed better performance than did the standard dry RF ablation. However, these two methods have a considerable risk of unexpected burn injury to the adjacent vital structures by the boiling saline, as several previous studies have demonstrated (11, 13, 33). Theoretically, the risk of burn injury related to the leaking of hot saline along the electrode and uneven spread of conductive saline along the paths of least resistance may be increased when using too high a volume or too fast an infusion rate. Therefore, further studies concerning the optimal of amount and concentration of the saline are warranted. Furthermore, there is one theoretical concern about wet RF ablation, i.e., saline, contaminated with viable tumor cells, may leak out of the electrode track and causes peritoneal or track seeding (33–35). Another equally unproven concern is that the saline may increase the intratumoral pressure and force tumor cells into the circulation, causing hematogenous seeding (34).

Our experimental study has certain limitations. First, all the ablations involved normal liver parenchyma, not tumor tissue, and they were performed in vitro. Living tumor tissue has a cooling “sink” effect due to the blood flow (36); thus, rapid heat exchange can occur. Therefore, the extent of extrapolation of the results of this experimental study to the real clinical situation is not certain. However, despite these considerations, our work provides a reliable model for comparative study on the efficiency of different RF systems. Second, following a procedure developed in earlier studies, we tested only 5% and 36% NaCl solutions. We believe that further experimental study aimed at optimizing the concentration and the amount of hypertonic saline solution is warranted.

In conclusion, wet RF ablation with infusion of 5% or 36% NaCl solution produced significantly larger ablation zones than the standard dry RF ablation or RF ablation with a preinjection of NaCl solutions. This higher level of coagulation necrosis produced by the wet RF ablation may be due to the combined effect of a greater delivery of energy, which is caused by good control of tissue impedance, and the better heat conductance. The increase of coagulation necrosis by wet RF ablation will likely be of benefit for clinical applications of RF tumor ablation therapy, and especially for a large size tumor.

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