Acta Radiologica Open
4(7) 1–3
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DOI: 10.1177/2058460115584111
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Comment to: Månsson C, Nilsson A, Karlson B-M. Severe complications with irreversible electroporation of the pancreas in the presence of a metallic stent: a warning of a procedure that never should be performed. Acta Radiologica Short Reports 2014;3(11):1–3.

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Date received: 7 March 2015; accepted: 5 April 2015

To the editor,

In an important case report (1), Månsson et al. described the severe complications, and subsequent death of a patient following irreversible electroporation (IRE) treatment of a 4 cm large, locally advanced pancreatic head carcinoma, with a self-expanding metallic stent placed in the common bile duct. The authors referred to a statement of the IRE equipment manufacturer that IRE "ablations close to metallic stents should be seen as a contraindication" because of fear "that metallic filaments in the stent should conduct the electricity and get hot". They also warned in their title that IRE "... of the pancreas in the presence of a metallic stent: a procedure that never should be performed" and in their conclusion "... we would like to warn others from repeating this possible mistake". The authors suggest a relation between the IRE procedure and the duodenal and colonic perforation discovered 2 months after IRE during emergency exploratory laparotomy, and 2 days after loop sigmoidoscopy.

The aim of our comment is to revisit the rationale that led to this warning. We will present two reasons which show that IRE pulses do not directly heat up a stent, the first, experimental, and the second, theoretical. However, indirect stent heating occurs by heat conduction from IRE Joule-heated tissue.

The first, experimental, reason is that we visualized the temperature distribution around a self-expandable nitinol stent of 4 mm diameter located between two IRE electrodes embedded in a tissue phantom, exposed to 90 pulses of 90 µs duration, 1.5 kV/cm, 1.5 cm active tip exposure, at repetition frequency 1.5 Hz (unpublished data). We found that the presence or absence of a stent did not significantly change the temperature distribution around the electrodes (Fig. 1).

The second, theoretical, reason is that, from a physical point of view, IRE pulses will not directly heat up a metallic object located between the IRE electrodes. This is a consequence of Maxwell's equations, named after the Scottish mathematical physicist James Clerk Maxwell (1831–1879), which describe how electric fields and magnetic fields are generated and altered by each

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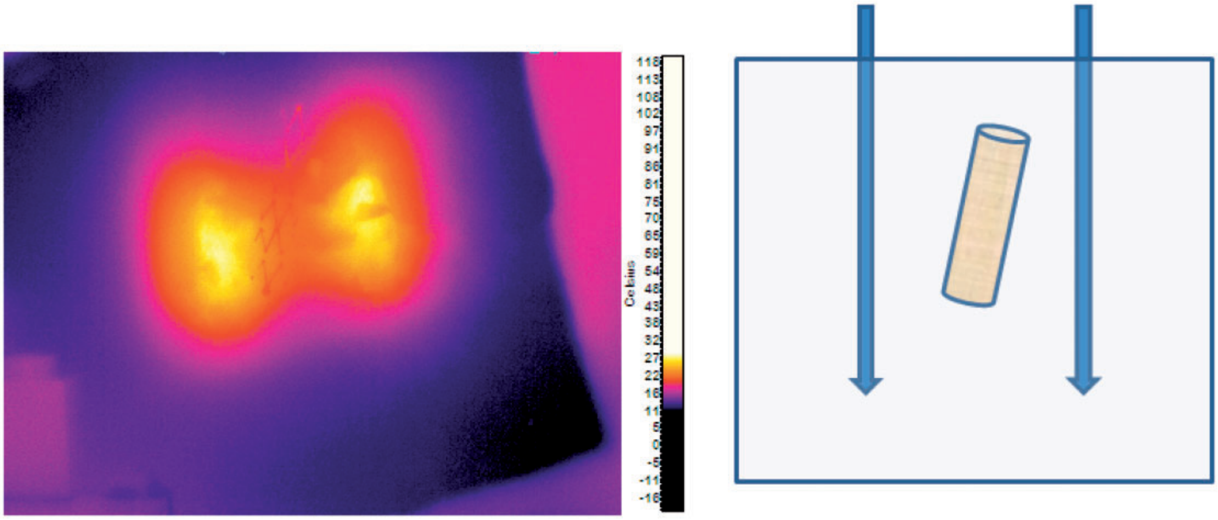

Fig. 1. Thermal image of the temperature field at the surface of an artificial tissue model, after 90 pulses of 90 μs duration, 1.5 kV/cm, 1.5 cm active tip exposure, at repetition frequency 1.5 Hz of IRE exposure. The self-expandable nitinol stent (length 4 cm, diameter 4 mm) is positioned just underneath the surface. The low temperature "shadow" of the stent can be appreciated against the higher background temperature. The highest rise is around 17.6°C above baseline temperate at the tip of the electrodes.

other and by charges and currents (details can be found at, for example, http://en.wikipedia.org/wiki/maxwell's_equations). First, static electric field lines are always perpendicular to a metal surface. Therefore, the component of the electric field parallel to the metal surface is zero, implying that an electric current cannot flow through the metallic stent so Joule heating cannot occur. However, an IRE pulse of about 100 μs duration cannot exactly be described by a static field. Such a pulse is equivalent to a spectrum of periodic electric fields. These time-varying electric fields generate time-varying magnetic fields which are perpendicular to, and have amplitudes proportional to, those of the electric fields. Such a periodic magnetic field causes Joule heating proportional to the magnetic field squared, see, for example, section 8.1 of Jackson (2). However, analysis shows this mechanism to have no noticeable thermal effect on metallic stents, e.g. for nitinol stents (an alloy of nikkel and titanium), by using dielectric permittivity of about 60 times the vacuum permittivity ($8.854 \cdot 10^{-12}$ Farad/m), based on Ti-oxide as Ti has high affinity for oxygen (3) (the dielectric constant of nitinol could not be found), and a magnetic permittivity of about the magnetic permittivity of vacuum ($4\pi \cdot 10^{-7}$ N/A^2) (4), electric field strengths of a few kV/cm and frequencies of up to about 30 kHz, associated with 100 μs IRE pulses. So, direct Joule heating of a metal stent during IRE procedures does not occur.

A metal object between IRE electrodes does however change the electric field distribution during an IRE-pulse and therefore the Joule heating of the tissue in response to IRE pulse sequencing (5–10). The calculated E-behavior along a line perpendicular to, and through the electrodes and metallic stent is shown in Fig. 2 with and without a stent (unpublished results by CWMvdG). Importantly, the metallic enclosure of the stent effectively acts as a Faraday-cage, shielding the biliary structures inside the stent from the electric field distribution outside the stent. Nevertheless, heat conduction from the much higher IRE-derived tissue temperatures near the electrodes causes increased temperatures of the tissue surrounding the stent, and hence also the stent itself, as has been explained previously (8).

Thus, a stent cannot become hotter than the highest tissue temperature at the tissue-stent interface.

Although IRE was initially introduced as being non-thermal, various publications have now demonstrated that significant heat generation occurs using the current clinical IRE settings (e.g. 70–100 pulses, 90 μs per pulse, ECG-triggered, 1.5 kV/cm) (5–10). Thus, although no details were or could have been provided by Månsson et al. (1) on IRE settings and needle positions used to treat their patient elsewhere, it is likely that the temperatures of tissue and stent were elevated in the pancreatic tissue volume enclosed by the needles. However, like the authors (1), we are unable to identify the exact course of events that led to abscess formation, bowel perforation, and pseudo-aneurysm formation, and whether passive stent heating from the hot tissue near the electrodes contributed to these complications.

Although we have shown that the previously accepted reason for metallic stent removal prior to IRE is invalid, i.e. IRE has no direct Joule heating

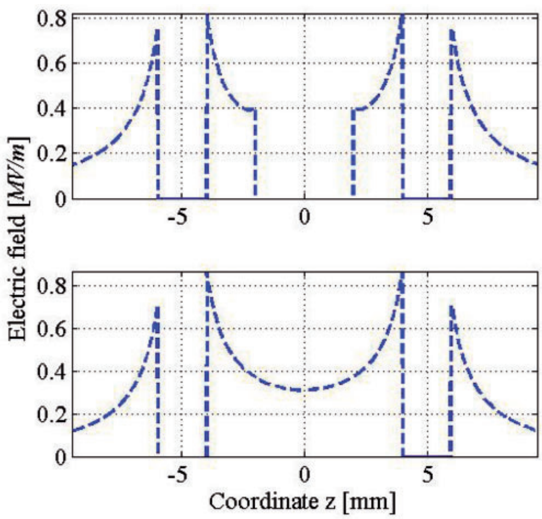

Fig. 2. Computed electric field (E) values (in 10^6 V/m) for the geometry of Fig. 1, here with 2 mm diameter electrodes, at 1 cm distance, and a 4 mm diameter metallic surface, representing the stent, along a line perpendicular to and through the electrodes and metallic stent. Voltage is 1.5 kV on the left electrode and -1.5 kV on the right electrode (thus 3 kV between the electrodes). Top: With stent and a maximum E of 0.82×10^6 V/m (0.82×10^4 V/cm). Bottom: Without stent and maximum E of 0.87×10^6 V/m (0.87×10^4 V/cm).

effect on a metallic stent, we cannot exclude that other reasons may justify stent removal. Some of these are: (i) a stent affects the electric field distribution, and hence the Joule heating, of the tissue enclosed by the IRE electrodes (Fig. 2); (ii) the Faraday-cage effect of a metallic stent (i.e. zero electric field inside the stent lumen) may affect the IRE therapeutic efficacy on cancer cells if present inside the stent; (iii) the lack of Joule heating inside a stent (Faraday-cage effect) and the possibility of having air bubbles affects the thermal response of the tissue to IRE; (iv) indirect stent heating occurring during IRE may affect the stent properties, e.g. mechanical strength. Therefore, if a metallic biliary stent is required we advise to use a retrievable fully covered stent (Wallstent) which can be removed easier than uncovered stents.

In conclusion, direct stent heating during IRE procedures does not occur. So, this mechanism cannot have caused the complications described by Månsson et al. (1). However, indirect heating obviously occurs by heat conduction from the IRE-heated tissue (5–10). To which extent this mechanism has contributed to (part of) the complications remains unknown. Further studies regarding the optimal procedure of pancreatic IRE in patients with a metallic biliary stent are required and are currently being performed by our group.

Conflict of interest

None declared.

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