Basic Science

Local temperature elevation as a marker of spinal implant infection in an animal model

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\textbf{Background:} Temperature elevation, a classic marker of infection and local temperature elevation, might be a useful predictor of early infection. However, temperature measurement around the spine is not readily accessible. The purpose of this study was to explore whether a temperature sensing implant might reproducibly detect local temperature change associated with peri-implant wound infection, in a rabbit model.

\textbf{Methods:} Twelve adult rabbits were implanted with a spinal screw-rod construct. Temperature probes were placed at the implantation site as well as at a separate scapular site away from the surgical site to serve as control. Animals were inoculated with S. aureus: group 1 (saline control), group 2 (low dose 1 × 10\textsuperscript{2} CFU/site), group 3 (medium dose 1 × 10\textsuperscript{4} CFU/site), and group 4 (high dose 1 × 10\textsuperscript{6} CFU/site) and monitored for 7 days prior to euthanasia.

\textbf{Results:} The scapular control temperature and implant site temperature in the non-infected animals remained similar throughout the study period. Both the scapular control and implant site temperatures were elevated in the infected animals compared to the non-infected animals. There was a statistically significant difference in the scapular control temperature and implant site temperature in all infected animals but not in the non-infected animals. Difference in temperature elevation between implant site and control scapular site were greatest for the animals with worst clinical appearance during the post-mortem evaluation.

\textbf{Conclusions:} This rabbit model demonstrates that local temperature measured in proximity to a spinal implant is elevated in the presence of infection with greater elevations associated with worse infections. Availability of an implantable temperature sensor may yield valuable information for the assessment and treatment of suspected spinal wound infection in the clinical setting.

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\textsuperscript{\ast} Summary: In a rabbit model, local temperature measured in proximity to a spinal implant was elevated in the presence of infection compared to a control site at the scapula; with greater elevations associated with worse infections. \\
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vated local temperature surrounding the implants might also be useful in differentiating between superficial and deep wound infection [7].

The goal of this study was to explore whether a temperature sensing implant might reproducibly detect local temperature change associated with peri-implant wound infection, in a rabbit model [8,9]. In particular, we sought to differentiate between infected and non-infected animals and between infected and non-infected sites within the same animal.

Methods

After receiving Institutional Animal Care and Use Committee Approval, twelve adult New Zealand white rabbits weighing at least 3kg were implanted with a multi-axial bone screw anchored in the L6 transverse process, a set screw and a titanium rod. A separate incision approximately 5” away from the surgical site at the scapula was also created to serve as a control site. Each animal had two separate intramuscular probes (IPTT-300, Bio Medic Data Systems, Seaford, DE) measuring temperature at these two discrete sites. Prior to closure, implant constructs in the “infected” group were inoculated with Staphylococ- cus aureus and the “non-infected” group were inoculated with saline. The animals were divided into 4 groups of three: group 1 (non-infected control with saline), group 2 (low dose of 1 × 10^6 CFU/site), group 3 (medium dose of 1 × 10^6 CFU/site), and group 4 (high dose of 1 × 10^6 CFU/site). No prophylactic antibiotics were administered. All animals were monitored for 7 days after implantation prior to euthanasia. Temperature readings were collected from both sites three times per day. White blood cell (WBC) counts and C-reactive protein (CRP) serum levels were determined at day zero and day six.

Post-mortem analysis included observational analysis of infection severity as graded by the veterinary staff. The severity of the infection was scored from 0 = no infection to 4 = severe infection (Table 1). Measurement of total colony forming units (CFU) from each wound site was also performed. Samples for CFU counts were taken from peri-implant tissue, spinal hardware and the temperature probe. CFU data was analyzed with HardyCHROM UTI agar (Hardy Diagnostics, Santa Maria, CA) and Tryptic Soy Agar (TSA).

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 27.0 (Armonk, NY). Repeated measures ANOVA was used to compare temperatures across the four animal groups over time. One way ANOVA was used to compare serum markers at Day 1 and Day 7 among the four groups followed by Dunnett’s Method to compare the Non-infected animals to the Infected animals.

Results

Non-infected animals remained asymptomatic during the course of the study, while infected animals inoculated with S. aureus had elevated temperatures at both the control scapula and implant site. Elevated temperatures peaked on Day 4 in all animals at all sites except for the control scapula in High Dose infected animals where the elevated temperature peaked at Day 5. Temperatures returned to normal on Day 6 (Fig. 1).

The scapular control temperature and implant site temperature in the non-infected animals remained similar throughout the study period. Both the scapular control and implant site temperatures were elevated in the infected animals compared to the non-infected animals (Fig. 2). Repeated measures ANOVA showed that there was no difference in the scapular site temperature over time between the infected and the non-infected animals (p=0.380) but that there was a significant difference in implant site temperature over time between the infected and non-infected animals (p=0.007).

White blood cell counts increased by 7% in the non-infected animals and increased 50% in the infected animals (Table 2) regardless of inoculation dose. Non-infected animals had a 30% increase in neutrophils compared to an 80% increase in the infected animals across all infected animals. CRP was elevated in all animals prior to euthanasia compared to pre-implantation. CRP levels were similar between the non-infected animals and the Low Dose infected animals. Post-hoc analysis showed that there was a difference in CRP levels between Medium and High Dose infected animals and the non-infected animals at termination. No bacteria were recovered from the implant site in the non-infected animals. TSA and HardyChrom™ UTI showed similar bacterial recovery across all infected animals regardless of initial inoculation dose.

Clinical Wound Infection Scores for each of the animals based on clinical appearance during the post-mortem evaluation and maximum temperature recorded over the study period is summarized in Table 3. CWIS depended on whether the animal was inoculated with S. aureus independent of the initial inoculation dose. Animals with the highest CWIS also had the highest maximum temperature over the study period. Scapular microchip incision site was macroscopically normal with no fluid or white matter across all groups.

Discussion

This experimental rabbit model serves as proof of concept that local temperature measured in proximity to a spinal implant is elevated in the presence of infection. Local temperature elevation was clearly different between infected versus non-infected animals and also between the infected spinal implant site and a control site within the infected animals. The largest between group difference (infected versus non-infected animals) was seen on Day 1 which may be reflective of an early systemic inflammatory response to the inoculum superimposed on the catabolic effect of the surgery [10, 11].

Not only were both the scapular control and implant site temperatures elevated in the infected animals compared to the non-infected animals, the implant site temperature was significantly higher compared to the scapular control temperature in all infected animals. This finding suggests that implant site temperature may differentiate site of infection versus systemic temperature elevation or as compared to a non-infected surgical site. The largest within animal temperature difference was seen on Day 2, suggesting that local temperature elevation may be a marker of early infection.

Although leukocyte and neutrophil counts were elevated similarly across all infected animals regardless of initial inoculation dose, CRP levels on Day 7 were higher in the infected animals with medium and large initial inoculation doses compared to those with no small initial inoculation doses. This suggests a dose dependent association between initial bacterial inoculation and level of CRP at termination. The temperature differential between the spinal implant site and the control scapular site was greatest in those animals with the most severe infection as graded by clinical appearance (CWIS ≥ 4).

Manifestations of infection in this model were consistent with clinical experience [2, 6]. Severity of infection is not adequately evaluated by a single marker, as clinical presentation is modulated by local factors such as soft tissue injury, and systemic factors such as immune response. In the clinical setting, WBC elevation might indicate either a more severe infection or a more robust clinical response. Minimal wound erythema might indicate a minor infection or potentially host immunodeficiency.

Particularly for patients with spinal implants, determining the severity of infection and specifically the presence of subfacial involvement may be difficult, but is critically important. Deep wound exploration is a substantial procedure which surgeons would certainly avoid if it were not necessary. On the other hand, untreated deep wound infection

| Table 1 | Clinical Wound Infection Score. |
|---------|--------------------------------|
| Score   | Percentage of Area Covered in White Matter |
| 0       | 0% |
| 1       | > 0 to 25% |
| 2       | > 25 to 50% |
| 3       | > 50 to 75% |
| 4       | > 75 to 100% |

| Results | |
|---------| |
| Non-infected animals remained asymptomatic during the course of the study, while infected animals inoculated with S. aureus had elevated temperatures at both the control scapula and implant site. Elevated temperatures peaked on Day 4 in all animals at all sites except for the control scapula in High Dose infected animals where the elevated temperature peaked at Day 5. Temperatures returned to normal on Day 6 (Fig. 1). |

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Particularly for patients with spinal implants, determining the severity of infection and specifically the presence of subfacial involvement may be difficult, but is critically important. Deep wound exploration is a substantial procedure which surgeons would certainly avoid if it were not necessary. On the other hand, untreated deep wound infection
The use of systemic temperature as the internal control would present a more relevant clinical comparison. Also, an antibiotic treatment arm might give some indication as to whether early identification of deep infection might facilitate treatment short of surgical exploration.

Conclusions

Despite these shortcomings, this study demonstrates the technical feasibility of local temperature measurement as a marker of peri-implant spinal wound infection in an animal model. It presents at least the possi-
Plot of Readings from Temperature Probes Between the Non-infected vs Infected Animals

![Graph showing temperature readings](image)

Fig. 2. Plot of readings from temperature probes from the non-infected vs infected animals. Numbers in bold font are temperatures at the implant site. Numbers in regular font are temperatures at the control scapular site. Bars signify the difference between the temperatures in the implant site compared to the scapular control site.

### Table 3
Clinical Wound Infection Score and Maximum Implant Site Temperature for each animal.

| Inoculation Dose | Animal ID | White Matter Score | Maximum Implant Site Temperature (°F) |
|------------------|-----------|--------------------|---------------------------------------|
| Non              | 59780     | 0                  | 39.4                                  |
| Infected         | 59781     | 0                  | 39.4                                  |
| Low              | 59782     | 0                  | 39.3                                  |
| Dose             | 59783     | 4                  | 40.9                                  |
| Medium           | 59784     | 4                  | 40.6                                  |
| Dose             | 59785     | 2                  | 40.4                                  |
| High             | 59786     | 3                  | 40.4                                  |
| Dose             | 59787     | 1                  | 40.2                                  |
| Dose             | 59788     | 4                  | 40.2                                  |
| Dose             | 59789     | 1                  | 40.4                                  |
| Dose             | 59790     | 3                  | 40.6                                  |
| Dose             | 59791     | 4                  | 40.6                                  |

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