Location matters when sampling a wound: The impact of fluorescence imaging on microbiological findings and its role in diagnostic & antibiotic stewardship

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Introduction

- Accurate diagnosis of infection status and a comprehensive microbiologic profile of a wound is essential to outline effective therapeutic plans.
- The role of microbiological analysis of tissue samples is well established but has limitations, such as subjective sample site selection, delayed results and technical variability.
- Diagnostic challenges lead to haphazard antimicrobial prescription, which strengthens antibiotic resistance.

Point-of-care **fluorescence imaging** (MolecuLight) informs on **the presence and location of high bacterial loads.** It is **4 times more sensitive** than clinical signs and symptoms (CSS) alone[1], it informs on the pertinence of sampling and guides its location. Using this technology helps improve healing rates and supports a more rational use of antimicrobials including systemic antibiotics.[1-3]

...but how has fluorescence Imaging impacted microbiological results in the real world?

Methods

Post hoc analysis of a 78-wound subset from the US Multi-site Fluorescence Imaging Assessment and Guidance (FLAAG) 350-wound clinical trial[1]

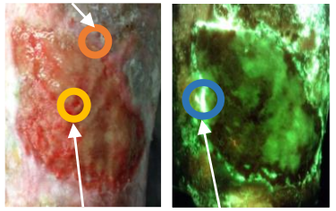
- All wounds had imaging performed and up to 3 punch biopsies taken for microbiological analysis. **All 78 wounds in this analysis had 2 biopsies taken**.
- The trial assessed standard of care (SoC) method of diagnosing high bacterial loads using clinical signs & symptoms of infection & inflammation vs. a fluorescence imaging device (MolecuLight).

The following patient assessment sequence was strictly followed to avoid bias:

1. Clinical evaluation of wound
2. Capture standard image
3. Select punch biopsy (tissue sample) site for microbiology based on SoC/CSS*
4. Fluorescence imaging and selection of additional biopsy site based of FL+ area(s)*
   - If SoC/CSS was different to the fluorescence-imaging area

The 3 Sample site options:

Clinical suspicion (CSS)*



Center of the wound (SoC)

Area of fluorescence-positive signal

Objectives

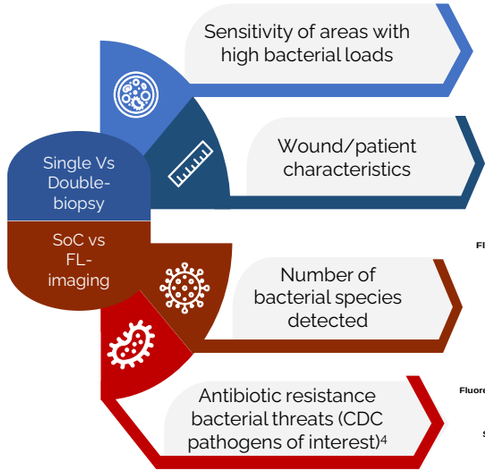
1. To determine **the characteristics** of the patients & wounds where an additional sample site (besides SoC/CSS) was taken based on FL-imaging by comparing:

Single-biopsy n=272 VS **Double-biopsy n=78**

2. To compare **the culture results** of double-biopsied wounds from sample sites selected via:

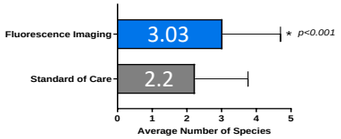
Standard of Care VS **FL imaging findings**

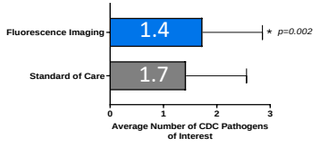
Results

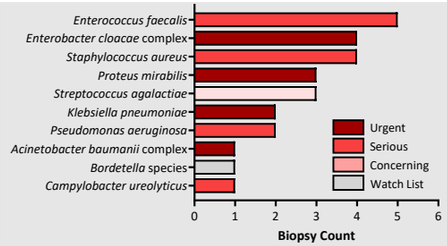


87.2% for SoC-guided biopsy Vs. 98.7% for FL-guided biopsy (p=0.0059)

- Wounds where a second biopsy site was deemed needed were significantly larger, deeper, & wider (p<0.02).
- Patients were similar in age and sex.







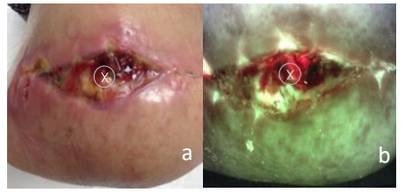
Graph (left) shows the most common pathogens detected by fluorescence guided biopsy that were missed by SoC sampling at the center of the wound:

Bars denote the number of FL informed biopsies where each pathogen was detected. Bar colors represent the categories of CDC pathogens of concern, per threat level.[4]

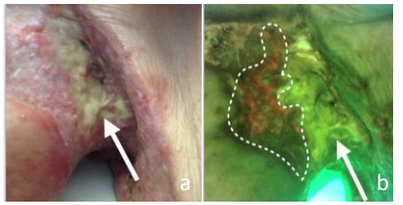
Clinical Cases and Discussion

Sample site selection

- Single-biopsies were all based on SoC per trial design. No biopsies were chosen based on CSS alone.
- It was noted that in smaller wounds, FL+ areas overlapped with SoC in the single-biopsy cohort 30% of the time.



Example of overlapping FL and Soc sample sites. Post-amputation wound. "X" denotes the location of the sample as per SoC & trial design. a) Standard image b) FL-image with a positive bacterial (red) signal around the center of the wound.



Non-healing burn wound exhibiting signs of infection. a) Standard image with arrow showing locations of 3 previous swabs that were negative, despite significant exudate from the region. b) FL-imaging demonstrated that area with high-bacterial loads was to the left of the clinically selected sample site (intermittent line). Microbiological report from a swab taken from the red FL area reported *E. coli* and *S. aureus*. Targeted treatment was successful.

Overcoming uncertainty and inaccuracy

FL-imaging was able to detect areas of high bacterial loads with a significantly higher sensitivity than SoC, which translated in capturing more pathogens, amplifying the scope of the microbiological analysis. Clinical assessment alone may provide an inaccurate representation of a wound microbial profile leading to a failed treatment.

Conclusions

- Microbiological analysis can be enhanced if its implementation is supported by more advanced diagnostic measures.
- Seeking optimization of the right diagnostic strategy for the right patient, at the right time, in the most efficient way to obtain more precise results has been named *diagnostic stewardship*. This is an essential partner to *antibiotic stewardship*.[5-10]
- Use of fluorescence imaging to inform biopsy location (if one is to be taken) is in line with diagnostic and antibiotic stewardship efforts. These efforts can have a worldwide impact on outcomes and in the fight against antibiotic resistance.

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References