Pilot clinical evaluation of surgical site infections with a novel handheld fluorescence imaging device

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INTRODUCTION

- Patients with abdominal wounds following colorectal resection and abdominal wall hernia repair have a higher risk of infection, significantly affecting quality of life. For example, colorectal resections are associated with a 4-25% acute surgical site infection rate, despite peri-operative best practices for prevention.
- Wound management of this patient cohort is resource intensive and has been associated with the over-prescription of empiric antibiotic treatments caused, in part, by delays in culture tests.
- Health care providers rely on traditional biomarkers of wound infection (pain, purulent exudate, crusting, swelling, erythema, heat), which are subjective and lack sufficient accuracy to effectively guide clinical decisions.
- To address this, we developed a handheld fluorescence imaging device for point-of-care hospital and home care use that rapidly visualizes and quantitatively tracks bacteria, wound healing and connective tissue remodeling of surgical sites based on intrinsic fluorescence signals - in real-time and without the need for contrast agents.

METHODS

- 7 male and female patients (median age: 53 yrs, range: 36-62 yrs) were imaged at St. Michael's Hospital (SMH) in an ongoing, REB-approved clinical trial (ClinicalTrials.gov ID: NCT01650571) and in accordance with Good Clinical Practice. Patients presented with abdominal wounds (midline incision, ileostomy) resulting from general surgery with known or unknown infection status.
- We evaluated the effectiveness of the imaging device in detecting subclinical bacterial contamination in these wounds and compared this with conventional assessment, noting whether patients were symptomatic of infection at the time of imaging.
- Sequential white light (WL) and corresponding autofluorescence (AF) images of each wound were acquired with the imaging device to track and document progression of wound size and bacterial load *in situ*, for up to 4 months.
- A total of 48 microbial swabs were obtained from wounds guided by fluorescence imaging and sent for independent (blinded) correlative microbiological laboratory analysis. Areas in and around wounds that were suspected of bacterial colonization or infection by AF light (detection of green or red fluorescent signals) were swabbed by clinical staff and sent for microbiological analysis.
- Swab culture results were semi-quantitatively classified as 'Normal Skin Flora', 'No Growth', 'Very Light', 'Light', 'Moderate', or 'Heavy' bacterial growth. To calculate sensitivity and specificity of fluorescence imaging, the region of the wound where the swab was taken was considered negative for pathogenic bacteria if the swabs were classified as 'Normal Skin Flora' or 'No Growth'. It was considered positive for pathogenic bacteria for all other swab culture classifications.
- Proprietary image analysis algorithms were implemented to quantify changes in wound bacterial load over time based on the AF image intensities for each wound.

RESULTS

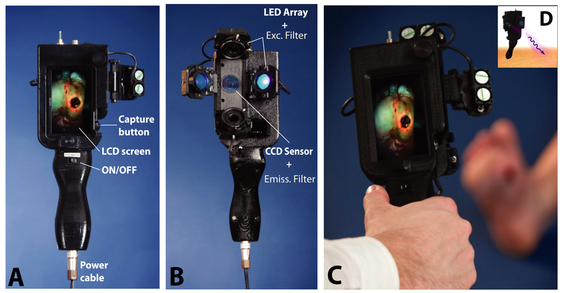

Figure 1. *Handheld prototype imaging device. (A) Fluorescence images are displayed in real-time on LCD screen. (B) Dual white light and violet LED arrays provide illumination of the wound, while the fluorescence emission filter is placed in front of the CCD sensor. (C) For illustration, the device is aimed at a diabetic foot ulcer to visualize the autofluorescence image on the viewing screen. (D) Illustration of the excitation LED illumination geometry.*

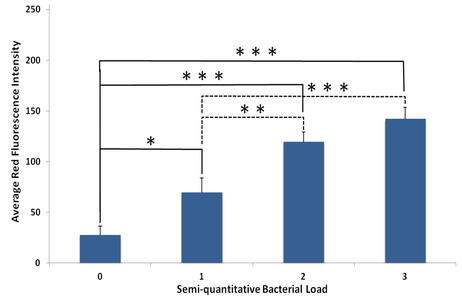

Figure 2. *Semi-quantification of bacterial load correlates with average red fluorescence intensity (n=68). This data is taken from a previous study. Average red fluorescence pixel intensity (scale 0-255) is greater when bacterial load is scored higher. Error bars are standard errors. ANOVA performed using Newman-Keuls. Legend: *= 0.05>p>0.01, **= 0.01>p>0.001, ***=p<0.001. Semi-quantitative scale: 0 – Normal flora, 1 – Light growth, 2 – Moderate growth, 3 – Heavy growth.*

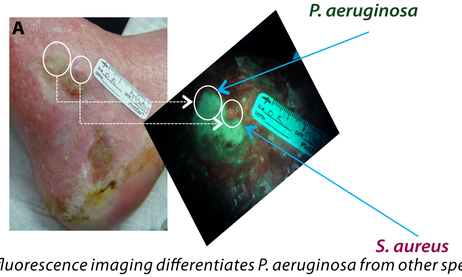

Figure 3. *Autofluorescence imaging differentiates P. aeruginosa from other species without contrast agents. (A) WL image shows chronic wounds, while (B) corresponding AF image differentiates between S. aureus (red colour) and P. aeruginosa (green colour) based on endogenous red fluorescent porphyrins in S. aureus and green fluorescent siderophores (e.g. pyoverdin) in P. aeruginosa. Adhesive ruler label: 3 cm.*

	Microbiological Analysis	
AF Image Red	+	-
+	33	2
-	8	5

$$\text{Sensitivity} = \frac{\text{True Positive}}{(\text{True Positive} + \text{False Negative})} = 0.80$$

$$\text{Specificity} = \frac{\text{True Negative}}{(\text{True Negative} + \text{False Positive})} = 0.71$$

Figure 4. *Sensitivity and specificity calculations based on 48 microbiological swabs. Fluorescence imaging has a sensitivity of 80% for detecting bacteria and a specificity of 71% for confirming the absence of bacteria.*

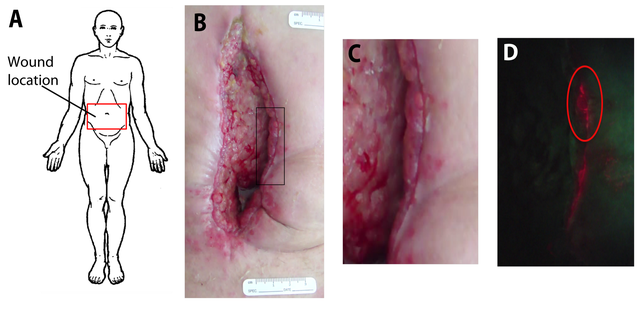

Figure 5. *Autofluorescence enables visualization of bacterial presence in wound peripheries missed by conventional methods. (A) Wound is located in the abdominal region. (B) WL image taken of the entire abdominal wound. (C) Close up of the wound periphery, which looks unremarkable. (D) The corresponding AF image (contrast adjusted: -10%) shows discrete areas of red fluorescence. The red ellipse indicates the area sampled. The swab came back as positive for pathogenic bacteria, with moderate growth of P. aeruginosa, mixed coliform bacilli, alpha-hemolytic streptococci and enterococcus species. Adhesive ruler label: 3 cm.*

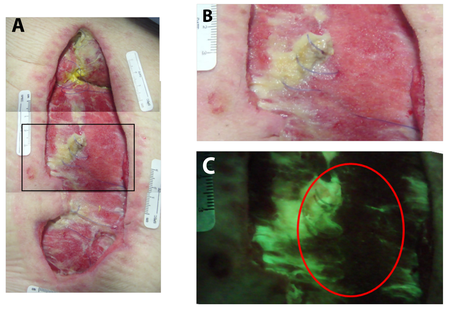

Figure 6. *The imaging device enables confirmation of the absence of pathogenic bacteria in the wound. (A) Stitched WL image of the entire abdominal wound. (B) Close up of the region where a swab was taken. (C) Corresponding AF image showing absence of characteristic bacterial red fluorescence. Red ellipse indicates wound area sampled yielding negative culture results for pathogenic bacteria, noting only light normal skin flora were present. Adhesive ruler label: 3 cm.*

CLINICAL HIGHLIGHTS

- Results show that fluorescence imaging safely enabled real-time visualization of discrete and focal areas of (otherwise occult) bacterial colonization in large (>1000 cm^2) midline abdominal wounds.
- The imaging device enabled guided sampling of bacteria in areas not conventionally swabbed by clinicians (e.g. the wound periphery), as part of standard wound care.
- Fluorescence imaging allowed accurate microbiological sampling of wounds with a sensitivity of 80% for detecting bacteria.
- This imaging approach confirmed the absence of bacteria (specificity 71%) in abdominal wounds of symptomatic patients, thereby validating the clinical decision to avoid unnecessary prescription of broadspectrum antibiotics for 2 out of 7 patients in this cohort at SMH.

SUMMARY OF FINDINGS

Real-time autofluorescence imaging of wounds:

- Is clinically feasible for use in abdominal surgical site infection assessment.
- Provides an instant and quantifiable image of bacterial presence, distribution and load, without the need for imaging agents.
- Enables image-guidance for:
  - Improving wound cleaning and debridement.
  - Targeted microbiological sampling.
  - Quantitative treatment response monitoring over time.
  - Confirming absence of bacteria from surgical sites, which could influence the clinical decision to prescribe empiric antibiotic treatments.

ACKNOWLEDGEMENTS

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