Minimally-Invasive Clinical Monitoring and Data Transference

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Introduction

- Electrocadioigraphy (ECG) is a technique used in clinical practice to record the electrical activity of the heart and aid in the diagnosis and monitoring of cardiovascular conditions e.g. Atrial Fibrillation1.
- Current ECG signal acquisition involves applying ‘wet’ electrodes to the surface of the skin where they transduce ionic potentials, generated by the heart, into electrical signals2.
- ‘Wet’ electrodes use conductive gels to facilitate signal transduction but over time the gel dehydrates, reducing the quality of recorded signals in long-term patient monitoring2.
- Microneedles (MNs) are minimally-invasive devices which circumvent the stratum corneum and directly contact underlying epidermal layers which are considered more conductive2. This negates the need for conductive gels and could improve the signal fidelity of ECG recordings.

Methods

- Through collaborative working, we aim to use ECG signal acquisition, as an exemplar, to assess the wearability and performance aspects of MNs for remote long-term patient monitoring.

Table 1: Summary of the physical features of 500µm polymeric MNs. Data presented as the mean ±SD (n=3).

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Width of array (cm)</td>
<td>1.8</td>
</tr>
<tr>
<td>Tip interspacing (mm)</td>
<td>1.63 ±0.03</td>
</tr>
<tr>
<td>Base interspacing (mm)</td>
<td>1.15 ±0.02</td>
</tr>
<tr>
<td>Length of MN (µm)</td>
<td>456 ±7.06</td>
</tr>
<tr>
<td>MNs per array</td>
<td>86 ±0.36</td>
</tr>
</tbody>
</table>

Figure 1: Illustration of the data transference process associated with remote health monitoring systems.

Figure 2: Light microscope image (a) and scanning electron micrograph (b) of uncoated, epoxy MNs prior to insertion into ex-vivo human skin.

Figure 3: OCT image demonstrating skin disruption resulting from MN application (a). En-face 2%w/v methylene blue staining following the application of an 87 microneedle electrode array to ex-vivo human breast skin (b). Sub-surface methylene blue staining of a 10µm section of MN treated ex-vivo human breast skin (c). Haematoxylin and eosin stained 10µm sections of MN treated ex-vivo human breast skin (d).

Figure 4: 50Hz notch filtered ECG signals acquired from an arbitrary waveform generator using a gain of x1 without the use of a resistor divider (a). 50Hz notch and 0.5-50Hz bandpass filtered ECG signals acquired from the arbitrary waveform generator using a gain of x24 and a resistor divider to simulate the low voltages of ECG amplitudes (b). The emitted ECG signal was generated at a sample rate of 250Hz with a peak R-wave amplitude of 1V and no DC offset.

Results

Table 1: Summary of the physical features of 500µm polymeric MNs. Data presented as the mean ±SD (n=3).

- MN Imaging
  - Polymeric MNs were imaged before and after skin insertion using light and scanning electron microscopy. MN parameters were measured using ImageJ.
- Skin Preparation
  - Subcutaneous fat was removed from ex-vivo human skin by blunt dissection. Skin was placed on conductive fabric and tensioned to two cork boards.
- ECG Recordings
  - Simulated ECG signals were generated through ex-vivo human skin and acquired using wet and MN electrodes. Data analysed using MATLAB R2018a.
- OCT Imaging
  - Optical coherence tomography (OCT) was used to image ex-vivo human skin before and after MN insertion. Acquired scans were analysed using ImageJ.
- Histology
  - Methylene blue dye was applied to skin after MN insertion. Biopsies were taken, fixed in formalin and cryosectioned. 10µm sections were stained with haematoxylin eosin.

Conclusion

Developing and validating a suitable ex-vivo ECG model will allow us to define those parameters which influence the wearability and performance of MN electrodes. Following optimisation we aim to compare the performance of the ‘gold standard’ wet electrode with the novel MN electrode in human volunteers.