Acceptability and Usability of Hollow Microneedle Drug Delivery Devices for the Treatment of Rheumatoid Arthritis

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ABSTRACT SUMMARY
A human factors/usability study was conducted to determine the acceptability of hollow microneedle delivery systems for use by patients with Rheumatoid arthritis (RA). RA patients, Rheumatoid nurses and Rheumatologists in the US and the UK were questioned about drug administration habits, pain perception and acceptable wear time for a microneedle patch system. Based on responses to 2D and 3D stimuli, preferences for elements of a microneedle delivery device were evaluated and represented in a prototype device.

INTRODUCTION
Rheumatoid arthritis is an autoimmune disease that affects over 1.5 million adults in the United States. This chronic disease affects the joints in the hands and the feet, causing painful swelling and eventually, joint deformity. RA patients may lose mobility in effected joints due to pain, swelling and joint deformity. RA affects 2-3 times more women than men and, although RA may occur at any age, it is most commonly first diagnosed in patients in their 60s (1, 2).

Although there is currently no cure for RA, there are a number of effective treatments including corticosteroids and several biologic drug products. In the case of the latter, administration is via either infusion at a clinic (e.g. Remicade®) or via self-injection with a syringe or autoinjector (e.g. Enbrel®, Simponi®, Humira®).

Previously, it has been demonstrated in-vivo that intradermal delivery of biologic drugs via, for example, microneedle based delivery devices, may result in faster absorption and increased bioavailability(3-6). Given the need chronic nature of RA and the relatively high cost of effective treatment via biologics, an administration route that can provide better bioavailability of the biologic API is a compelling idea with potentially significant economic ramifications.

Current research indicates that non-compliance associated with administration of injectable biologics prescribed for chronic disease, generally, and for the treatment of RA, specifically, is 10% (7-9), with needle phobia playing a significant role in noncompliance. Approximately 10% of all Americans are needle phobic and an even greater percentage cite their dislike of needles as the reason for forgoing medical treatment (10).

Several studies have been conducted to better understand the acceptability of microneedle-based delivery devices for delivery of chronic therapies or vaccines (11, 12). This study was designed to better understand the general acceptability of microneedle delivery in RA patients and, specifically, to gain insight on acceptability of 2D and 3D microneedle device stimuli to guide device development.

EXPERIMENTAL METHODS
Thirty eight RA patients (19 UK, 19 US), 7 Rheumatoid nurses (3 UK, 4 US), and 8 Rheumatologists (3 UK, 5 US) were interviewed 1:1, about drug administration habits and associated emotions and general usability of delivery systems. Subjects were shown 2D and 3D microneedle drug delivery stimuli and asked to evaluate their impressions of the devices represented, as well as subsystems of the devices (application, indicators, etc). Subjects were questioned about their impressions of and the acceptability of microneedle-based delivery systems for administration of RA drugs. Interviews were transcribed and videotaped and the data analyzed for elucidation of trends or tabulated in the case of quantitative responses. No injections/deliveries were performed in this evaluation, although subjects were asked to simulate injection with the 3D stimuli on a thin pad placed on the application site. Background data including current medication administration routines and disease history were collected and compiled at the beginning of each interview.

RESULTS AND DISCUSSION
Factors Effecting Compliance
Unpleasant administration experiences (pain or shock) can affect a patient’s willingness to take their medication. The unpleasant experience may be caused by the pain of delivery, a loud or unpleasant noise upon delivery, or a visual mark on the skin. Patient’s willingness to take their drug is also adversely effected when they are not confident on how to use the device or if they are not confident in the device itself (robustness). When the administration experience is unpleasant, patients may avoid taking the medication altogether or may “self-prescribe” a partial dose in an effort to minimize the unpleasant effects.

Acceptable Duration of Injection
Twenty three of the 38 patients were asked about the duration of administration they would tolerate. Ninety-five percent of those interviewed indicated that they would tolerate an infusion time of 5min or more; 57% said they would accept an infusion time of up to 15 minutes. Subjects who currently travel to a clinic for infusion of medication indicated they would tolerate a delivery time of up to 1 hour if they could self-administer
their medications at home. A summary of these data are provided in Figure 1, below.

**Figure 1. Max Acceptable Delivery Time, RA Patients**

![Bar chart showing max acceptable delivery times](image)

**Acceptability of Microneedle-based Delivery Device**

In response to the 3D stimuli, 32 of 35 subjects indicated that they would prefer to use a microneedle-based delivery device over a standard autoinjector. The device stimuli were perceived to be more comfortable, easier to use and less threatening. Patients responded favorably to features of the stimuli that increased robustness and provided a very simple, intuitive application procedure. Adhesion of the device to the skin during administration was also acceptable to subjects as long as the adhesive was gentle to skin.

**CONCLUSION**

Human factors studies such as this one provide important insight into patient’s mechanical and emotional response to drug delivery devices. This feedback, in turn, may provide information on how to improve patient compliance and on how to design a delivery device that will be used readily and correctly by specific patient groups. This study indicates that microneedle-based delivery devices that require skin adhesion have a high acceptability to RA patients, so long as the devices are easy to use and robust. With this patient population, the microneedle device stimuli shown were perceived as easier to use and less threatening than autoinjectors. This preference was consistent across subjects interviewed in the US and in the UK.

**REFERENCES**