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Usability evaluation of intradermal adapters (IDA)

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ABSTRACT

Intradermal adapter device technology minimizes the complexity of the Mantoux technique, thereby providing predictable, reproducible intradermal (ID) injections and removing the concerns regarding the ease and reliability of Mantoux technique when using conventional needle and syringe. The technology employs a simple device with geometry designed to gently deform the skin surface and the subcutaneous tissue, providing the ideal angle and depth of needle insertion for consistently successful intradermal injections. The results of this development were presented at the First, Second and Third Skin Vaccination Summits in 2011, 2013 and 2015 respectively [1,2,3].

The current publication addresses the performance of intradermal adapters (IDA) evaluated in three preclinical studies. The evaluations were based on the assessment of bleb formation in a skin model, an accepted indicator of ID injection success. All evaluated devices share the same proprietary dermal interface technology. Devices instituting this design are easy to use, require minimal training, and employ conventionally molded parts and cannula.

These studies evaluated IDAs of initial design integral with luer lock needles, IDAs for use with conventional syringes, and intradermal adapters for use with auto disable syringes (ADID adapters). The evaluated ID adapters were intended to consistently place the lancet of the needle at a depth of 0.75 mm from the skin's surface. This placement depth addresses the variation in the skin thickness at immunization sites for the majority of patients independent of many other variables.

Most participants preferred the intradermal adapter method over the traditional Mantoux and identified a need for the adapter at their workplace. Evaluation of IDAs by registered nurses indicated these devices increase success of bleb formation. The use of IDA increased the success of forming blebs by about 30%. Nurses felt the injections were much easier to perform, in particular by novices.

1. Introduction

There are many options for vaccine delivery including intramuscular (IM), subcutaneous (SC), and intradermal (ID) injections and nasal, oral, and transcutaneous methods. IM and SC are the most common routes of delivery. However, the ID vaccination offers several advantages. Skin contains a higher concentration of antigen-presenting cells processing and presenting antigens. These cells are critical components of the adaptive immune system response. The delivery of vaccines into the skin may lead to superior immune responses when compared to IM or SC [4].

There are other potential benefits associated with ID immunization. High immune response of the skin could lead to reduced number of required injections, rapid buildup of immunity, reduced number of office visits. Furthermore it could enable buildup of immunity in immunocompromised patients and elderly. The superior immune response may reduce the need for adjuvants for some vaccines. The use of ID vaccination also improves economics and logistics leading to dose sparing and minimized cold chain. These are the reasons ID vaccination is common in the developing world. Furthermore ID vaccination could increase availability of vaccines with limited or expensive antigens.

ID injections are typically administered using the Mantoux technique [5], which requires special training. While Mantoux was developed for TB testing over 100 years ago it remains the main technique for ID vaccination.

Contemporary nurses have to learn and use a broad range of techniques. Unfortunately, Mantoux is difficult to perform, particularly if the vaccinator's experience is limited as is often the case. Even vaccinators experienced in Mantoux risk improper depth of delivery, which is accentuated if the patient moves. Concerns have

Abbreviations: AD, autodisable; ADID, autodisable, intradermal; ID, intradermal; IDA, intradermal adapter; IM, intramuscular; LL IDA, luer lock needle with a mounted ID adapter; SC, subcutaneous.

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been reported on the difficulty of correct implementation of Mantoux, the needed time, the required training, and the potential resulting variability. These factors present a challenge to vaccine manufacturers who are considering the use of ID injection as a delivery method for current or new vaccines.

Despite multiple benefits we observe a slow rate of ID adaption. This situation is driven by difficulty with learning and reliably performing manual intradermal injection technique leading to poor trial implementation and resulting in inferior response when compared to IM dosing. Uncommon injection technique (ID) requires training and experience. The shallow insertion angle of 5–15-deg enables the lancet to be placed correctly in the relatively thin skin. The injection will not produce adequate results if the needle is placed too deep resulting in SQ delivery or too shallow leading to leakage. The needle bevel is visible just below the skin surface when the insertion is performed correctly. A bleb 6–10 mm in diameter appears over the needle bevel when the injection of .1 ml is performed correctly.

IDA technology brings the complexity of ID injections in line with conventional SQ injections performed by nurses daily. Risks to the variability of clinical results based upon the injection technique between sites and/or investigators is minimized. Furthermore IDA simplifies simultaneous ID vaccination at multiple sites. The multiple site vaccination approach was initially introduced for rabies to rapidly build immunity and is currently evaluated with a number of compounds in development.

The IDA holds the needle shaft parallel to the skin's surface at a consistent depth as the needle penetrates the skin, ensuring the lancet is placed into the skin to the correct depth of .75 mm [6]. This device reduces intradermal injection complexity and required training and increases repeatability. It is an inexpensive and simple single molded device which is intended for one-time use only. IDA aids the vaccinator, minimizes training needs and increases reliability and repeatability of the correct needle placement. The goals of improving seroconversion, reducing the cost per dose and speed to market are best achieved by using the currently available vaccine vials and syringes and this add-on ID adapter.

Conducted preclinical studies showed a consistent increase in the success of bleb formation using an adapter and Mantoux as compared with the unaided traditional Mantoux technique.

2. Methods

The usability evaluation was conducted on a freshly excised pig skin by injecting .1 ml of saline and evaluating the resulting bleb size.

2.1. Evaluation methodology

The usability evaluation of three different ID adapter prototypes was conducted on freshly excised pig skin, a skin model closely resembling the functionality of human skin. The excised pig skin was provided by a qualified supplier, Midwest Research Swine [7]. The excised skin was placed in custom frames (Fig. 1) preventing the skin shifting during the evaluation.

The evaluations were conducted by practicing nurses with varying level of expertise and experience. Recruited nurses worked in the proximity to the study sites. The recruitment target was to achieve an age distribution between 18 and 70 and to include both male and female nurses. The participation was voluntary with nurses receiving compensation for their time. Additional information on the participants is provided below along with details of a particular study.

Each nurse received a frame with a mounted sample of the pig skin (Fig. 1). Nurses injected 0.1 ml of saline into the skin during the usability studies. Intradermal injections of volumes over .1 ml

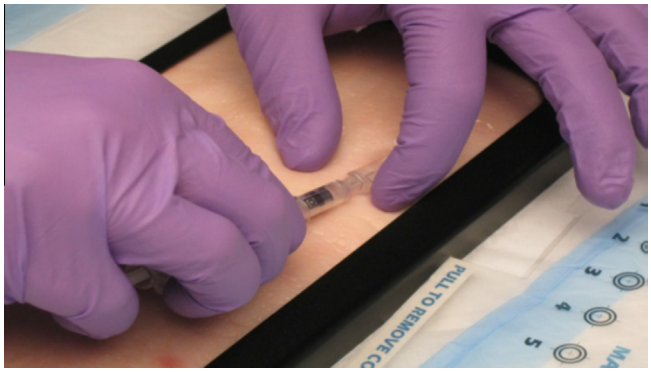

Fig. 1. Excised pig skin in custom frames preventing the skin shifting during the evaluation.

are not commonly practiced due to an increase in the pain level while .050 ml volumes are used primarily in pediatric patients. While participating nurses were practicing injections in their work and have received Mantoux training in school their experience in the Mantoux technique ranged from novice to proficient to experts. ID injection using Mantoux was judged by nurses to be twice as difficult as IV. This assessment reflects the infrequent use of ID in medical practice and the difficulty of its reliable and repeatable implementation while using unaided standard syringes.

Freshly excised pig skin is a widely accepted skin model. Nevertheless many nurses expressed difficulty acclimating to the unfamiliar pig skin. Users voiced that the skin was much tougher than human skin and also slippery. Due to the nature of the injection site, the results may vary from actual injection in humans.

The freshly excised pig skin is characterized by a slow diffusion of the injected saline due to the absence of blood flow. The bleb size does not change for an extended period of time prior to diffusing slowly. The bleb measurements were taken after the completion of a particular series on injections. For example during IDA evaluation pictures were taken after each of the 10 injections with a particular method were completed. The still photos of the skin were taken with a ruler and were used to determine the bleb size. The delay from the first to the last injection in the series was less than 20 min.

The bleb size is broadly accepted as a surrogate for the quality of ID injection. Incorrect intradermal injection could be associated with needle bevel placed too deep leading to subcutaneous administration. Alternatively the needle bevel could be placed too shallow leading to saline loss on the skin surface or wet injection. In either case the injection quality is reflected in the recorded bleb size.

Each usability study had a conventional Mantoux arm used as a comparator. The IDA and Mantoux method were presented to participants in an alternating order to reduce the order bias. Furthermore all evaluations were managed by Insight Product Development of Chicago, IL [8]. Insight has substantial experience in conducting usability studies for novel medical devices.

2.2. Devices

Three different prototype designs of the intradermal adapter were evaluated. The initial design developed by SID Technologies employed a Luer Lock needle with a permanently attached ID adapter section (LL IDA). It was an early adapter design which lacked some of the adapter features developed subsequently.

The luer lock needle assembly employed as a base Terumo Corporation safety needle *SurGuard2* with ½″ long, gage 27 needle. The safety component was removed and replaced by a permanently mounted ID adapter (see Fig. 2). The clear ID adapters were printed by stereolithographic technique. The adapters were mounted by an

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