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Clinical performance and safety of the ID adapter, a prototype intradermal delivery technology for vaccines, drugs, and diagnostic tests.

Courtney Jarrahian[a*], Darin Zehrung[a], Eugene Saxon[a], Emily Griswold[a], Leslie Klaff[b]

[a]*PATH, 2201 Westlake Avenue, Suite 200, Seattle, WA 98121, USA*
[b]*Rainier Clinical Research Center, 723 SW 10th ST, Suite 100, Renton, WA 98057, USA*

Abstract

Several vaccines, diagnostic tests, and medications are currently delivered intradermally, and it is likely that this route of administration will grow in importance. A phase I clinical study was conducted to evaluate the intradermal (ID) adapter, a prototype intradermal delivery aid, for safety and precision of injection. Healthy adult volunteers received two injections each of 0.1 mL of sterile saline solution in the upper deltoid region of the arm using the ID adapter. Injection performance was determined by the proportion of injections delivered to the dermal layer by measuring wheals and fluid leakage, and through ultrasound imaging. Of the 40 study injections, 100% were determined to be successful intradermal injections. Leakage of liquid at the injection site was negligible. Performance was similar with the bevel orientation both upward and downward. Minor bleeding and skin abrasions were the only reported adverse events. Injections were well tolerated based on self-reporting of pain of injection. Based on these results, the ID adapter appears to be safe and effective as an alternative to the Mantoux method of ID delivery for future use in clinical evaluations of ID delivery of vaccines, skin tests, and other drugs.

Keywords: Intradermal; Mantoux; vaccination; delivery technology; ultrasound

1. Introduction

One vaccine of importance to global public health is nearly universally delivered intradermally. Bacille Calmette Guerin (BCG) vaccine, used mainly in neonates to prevent tuberculosis, is given to approximately 100 million children each year [1]. Other existing vaccines are increasingly being delivered intradermally, including rabies and inactivated influenza vaccines; these are used in a wide range of age groups. Other vaccines are likely to be given intradermally in the future, including new-generation tuberculosis vaccines (based on BCG or modified vaccinia Ankara [MVA]), inactivated poliovirus vaccine, and possibly inactivated hepatitis A, hepatitis B, and live attenuated yellow fever [2]. For some vaccines, the choice of the intradermal (ID) route is due to increased safety and/or

* Corresponding author. Tel.: +1-206-285-3500; fax: +1-206-285-6619.
E-mail address: cjarrahian@path.org.

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effectiveness and, for others, the ID route offers increased immunogenicity in hard-to-vaccinate populations and/or enables dose sparing of vaccine to reduce costs or increase access.

ID injection is also used for diagnostic skin tests (e.g., tuberculin sensitivity test for tuberculosis and allergy tests) and to deliver some local anesthetics for medical procedures such as in dermatology.

The Mantoux technique [3] is the conventional method of performing an ID injection. It requires the syringe needle to be inserted at a 5° to 15° angle from the skin surface, through the stratum corneum and into the dermis of the skin, to a depth of approximately 1 mm from the skin surface. For tuberculin testing, the US Centers for Disease Control and Prevention (CDC) recommends using a tuberculin syringe with a 27 gauge, ¼- to ½-inch needle and short bevel [4]. For ID rabies vaccination in other countries, such as India, an insulin syringe is commonly used [5]. The standard practice for performing an ID injection using the Mantoux method is with the needle bevel oriented up [6] [7]. Slow injection of liquid (usually 0.05 ml or 0.1 ml) into the dermis produces a raised, blanched wheal, with a characteristic “orange peel” appearance. This is the clinical sign commonly used to denote a successful ID vaccination, and a 6-mm to 10-mm diameter wheal is considered typical for a 0.1 ml injection for tuberculin testing [8].

The Mantoux technique can be difficult to perform reliably, even with training and especially without experience and frequent use [9]. Improper ID injection technique can affect the results and safety of vaccination or diagnostic testing [10-13]. The ID adapter was designed to be an easy-to-use, potentially low-cost aid to facilitate ID injections with currently available needles and syringes by limiting the depth and angle of the needle as it penetrates the skin and by limiting the length of the needle shaft in the skin. The ID adapter used in this study is an investigational

Figure 0. Prototype intradermal adapter attached to a syringe with a 29 gauge, ½-inch needle, as used in this study.