DermalDose

Intradermal drug delivery made easy

11 november 2014 – University of Twente

Ir. Nol Brouwers
Luuk Jansen Bsc

What do we do?

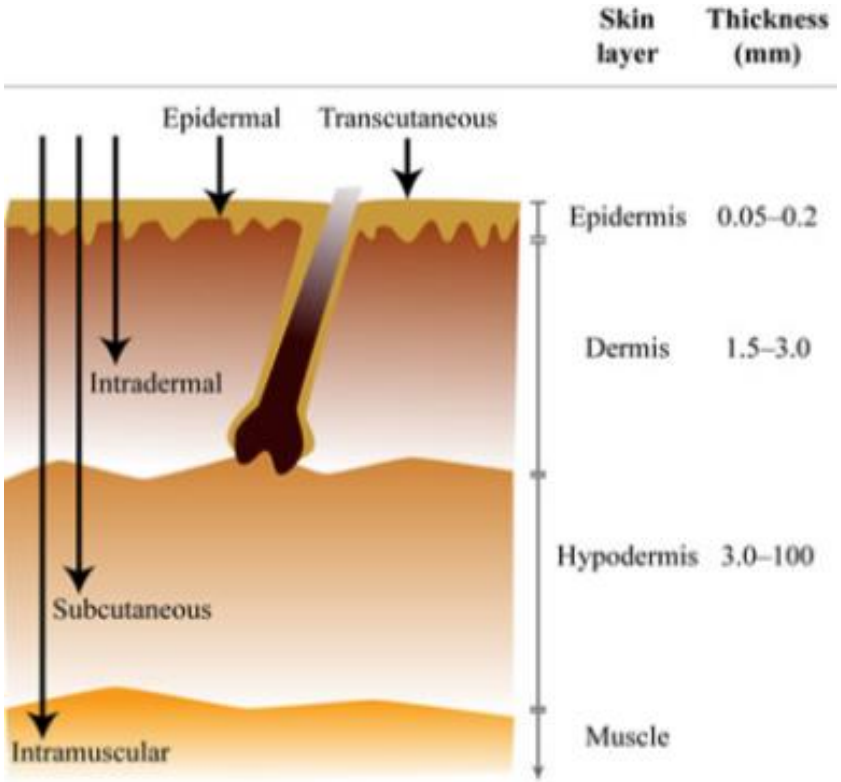
We develop and deliver DermalDose, a patented alternative for syringes, to pharmaceutical industries

Our mission, is to deliver a convenient and accessible method for intradermal drug delivery to people all over the world, by offering a user-friendly solution with great attention for reliability, precision, comfort and durability.

DermalDose
Intradermal drug delivery made easy

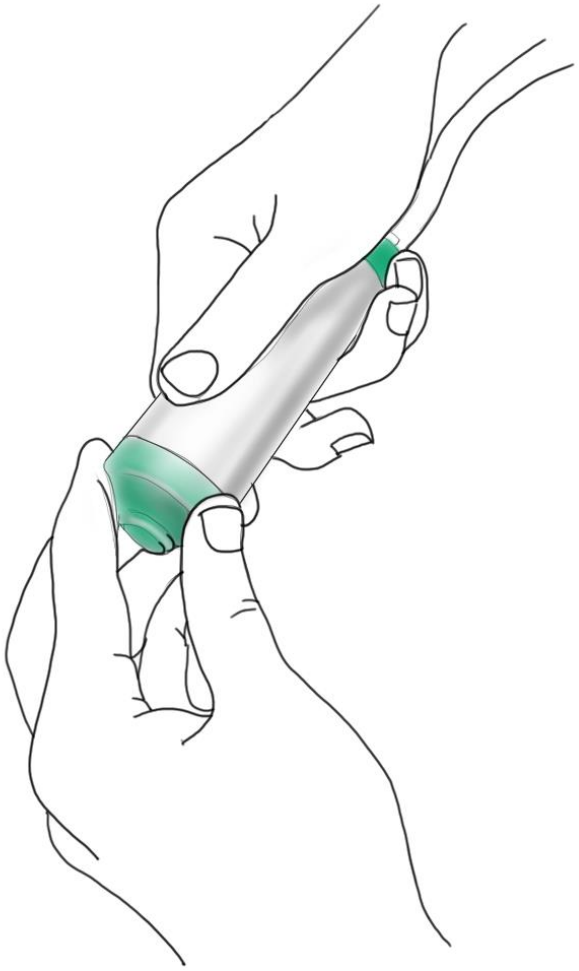
Intradermal drug delivery (IDD)

- Drug delivery in the dermis
- Has many advantages over regular injection methods according to literature
- Current ID injections are regularly given, but:
  - Hard to perform
  - Painful
  - Only in clinical situations



DermalDose
Intradermal drug delivery made easy

The DermalDose system



- Patented ss hollow microneedle based solution for IDD
- Injection at a depth of 900 µm
- Precize and reliable delivery.
  - Volumes between 5 and 100 µl
- Designed for self-administration and home-use
- Fast delivery in less than a second

DermalDose
Intradermal drug delivery made easy

DermalDose and IDD

Literature study on the use of hollow microneedles for IDD:

Advantages and disadvantages with regards to:

- Compliance;
- Pharmacokinetics;
- Children;

Can DermalDose be applied for the delivery of Methotrexate?

DermalDose
Intradermal drug delivery made easy

Compliance

- 25% of patients admit omitting or underdosing injections due to needle phobia. [2]
  - Prof. van Riel believed this to be 40% amongst Methotrexate users
- Microneedle insertion found to be significantly less painful than s/c catheters or hypodermic needles [1][2]
- Microneedles show no infections, little skin irritation and no bleeding [1]
- Self administration discontinuation is reported to be caused by:
  - intolerance to injections;
  - needle phobia;
  - side effects as nausea and vomiting;
  - sloughing at the injection site;
  - social difficulty to integrated in daily activities, or with friends, or in public area's [1]
- Nausea can occur anticipatory a day before medication, till 24 hrs after medication, in total of 3 days. [1]

DermalDose
Intradermal drug delivery made easy

Compliance

- Less skin trauma and injection site healing was faster with micro needle injections [3]
- Historically IDD injections were not attractive regarded difficult, unreliable, and not suitable for self administration. [4]
- Skin erythema caused by microneedles was small and disappeared in 2,5 hrs. [4]
  - After cathether treatment erythema was significantly greater
- IDD is alternative to oral or parenteral routes for reasons such as bad taste, drug degradation, first-pass metabolism, hepatotoxicity, pain of injections, emotional traumas and **improved patient compliance**. [1]
- Applicators must be designed for ease of use, convenient carriage, simplicity for self-administration, re-usable and low cost [1]
- **Concluding: all sources speak of a need for a consistent, reliable and comfortable IDD device for self-administration**.

DermalDose
Intradermal drug delivery made easy

Pharmacokinetics

- The uptake properties of IDD delivery have not been studied well due to difficulty to directly and reliable accessing the tissue bed by mechanical means. [5]
- Hollow ss micro needles succesfully delivered human doses of etanercept to swine, without effect on drug stability. [5]
  - Domestic swine demonstrates similar intradermal pharmacokinetics to human beings. [2]
- IDD results in faster uptake of drug compared to S/C delivery
  - Insulin peak was 30 min and 40% faster than s/c, the offset time was 100 min and 24 % faster than s/c[2]
  - Tmax value for ID was 37% of the s/c Tmax time and the Cmax value for ID was 130% of the s/c Cmax. (insulin)[4]
  - The time to max. concentration was 71% lower, and the maximum concentration was 191% higher compared to the s/c route. (etanercept in swine). [5]

DermalDose
Intradermal drug delivery made easy

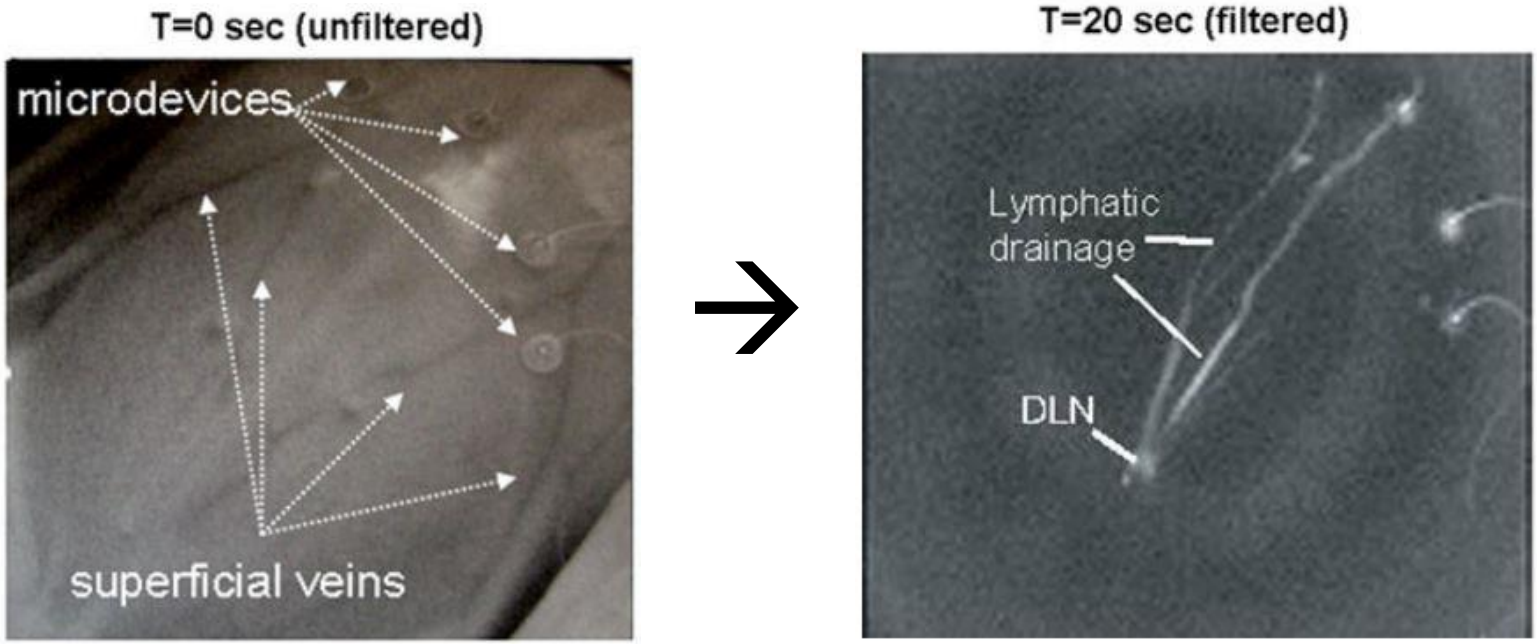
Pharmacokinetics

- Blebs from the µNeedles absorbed within 2 hours without any pain [2]
- The dermis is highly perfused with vascular and lymph capillary networks [5]
- The reason for accelerated pharmacokinetics is believed to be the rich capillary bed found in the superficial dermis or via lymphatic drainage [2]
  - Utilizing the lymphatic pathway intradermal delivery may provide faster access to the systemic circulation, especially for larger molecules. [3]

DermalDose
Intradermal drug delivery made easy

Pharmacokinetics

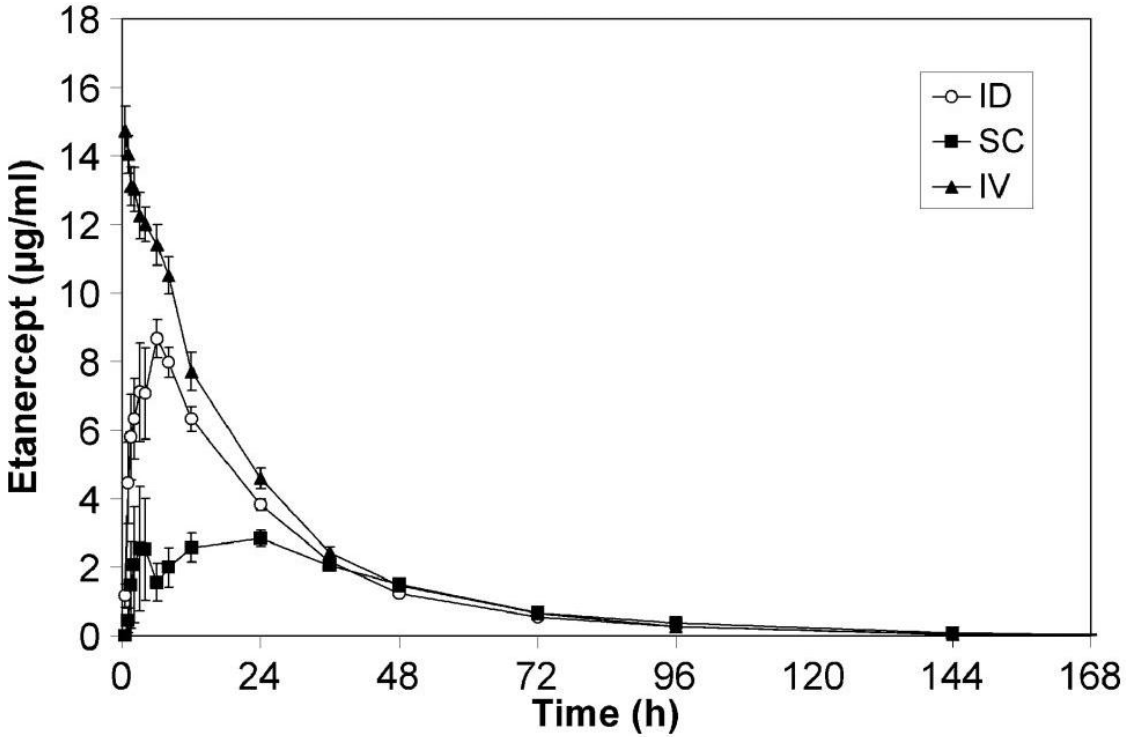
- ID delivery resulted in immediate uptake by the local lymphatic vessels as shown. [5]



DermalDose
Intradermal drug delivery made easy

Pharmacokinetics

- Etanercept microneedle administration demonstarated substantially higher bioavailability than the traditional S/C route. [5]



DermalDose
Intradermal drug delivery made easy

Pharmacokinetics

- Data reported by Harvey et al. comparing SC delivery with IDD. [5]

			ID	SC
Ethanercept	T_{max}	hr	5.21±2.20	17.80±9.7
	C_{max}	ng/ml	9,002±1,884	4,657±3,375
	Bioavailability	AUC/IV AUC	75	50
Somatropin	T_{max}	hr	0.47±0.25	2.75±0.46
	C_{max}	mIU/ml	612.60±187.10	158.50±31.00
	Bioavailability	AUC/IV AUC	101	109
Insulin	T_{max}	min	25.00±6.45	61.00±20.74
	C_{max}	µIU/m	117.51±56.01	31.76±10.58
	Bioavailability	AUC/IV lispro AUC	67 (lispro)	48

DermalDose
Intradermal drug delivery made easy

Children

- Children present with juvenile idiopathic arthritis (JIA) from 1 to 2 years of age benefit from a system that is less painfull and has less impact on daily activities. [1]

- Babies and children below the age of 8 years are considered to be more susceptible to skin irritation. [1]

DermalDose
Intradermal drug delivery made easy

DermalDose and ID delivery

- Huge gain in terms of compliance:
  - Comfortable injection to relieve patients from injection stress and pain
  - Design adjusted to needs of severe rheumatic patients
  - Designed for self-administration by uneducated people and elderly
  - Offers a platform for home healthcare
  - Connectivity with pharmacy, doctors or external devices possible
  - Able to inject a partner/family member without “needle fear”
  - No skin damage
- Results show efficient transport of medicine through the body
- Results show a better uptake of drug via dermis tissue
- Potentially less acting substance needed to obtain same effect
- Consistent ID delivery is new to the market, knowledge and research will expand when it arrives.

DermalDose
Intradermal drug delivery made easy

References

1. Uptal U. Shah, others, Michael Beresford Needle-free and microneedle drug delivery in children : a case for disease-modifying antirheumatic drugs (DMARDs) Int. Journal of Pharmaceutics 416 (2011) 1-11

2. Normann JJ, Brown MR, et. Al Faster Pharmacokinetics and increased patient acceptance of ID insulin delivery using a single hollow micro needle etc. : Pedriatic Diabetes 2013 : 14 : 459 - 465

3. Scott A.Burton, Chin-Yee NG, et. Al Rapid Intradermal Delivery of Liquid Formulations Using a hollow microstructured array. Pharm Res (2011) 28 : 31 – 40

4. Jyotii Gupta, Eric l. Felner, et al. Rapid Pharmacokenitics of ID insulin administered using microneedles in Type Diabetes subjects. Diabetes technology & Therapeutics volume 13, number 4, 2011

5. Alfred J Harvey, Scot A. Kaestner, et.al. Microneedle- based Intradermal Delivery Enables Rapid Lymphatic Uptake and Distribution of Protein Drugs : Pharm. Res. (2011) 28: 107 – 116

DermalDose
Intradermal drug delivery made easy