A FULLY FUNCTIONAL CLOSED-LOOP SYSTEM USING ULTRASOUND IMAGING TO AUTOMATICALLY DETECT LIPOHYPERTROPHY IN PEOPLE WITH INSULIN DEPENDENT DIABETES

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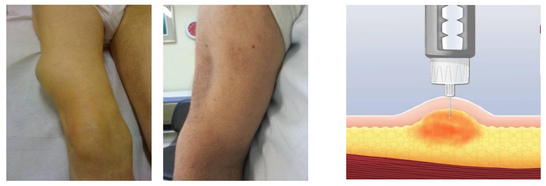
PROBLEM

What is Lipohypertrophy?

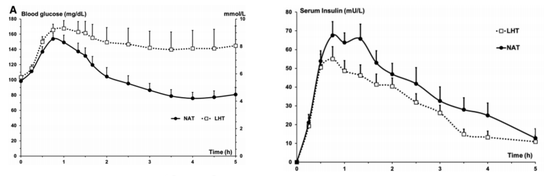
- Lipohypertrophy is a medical condition that refers to a lump creation under the skin caused by accumulation of adipose tissue at the site of many subcutaneous injections of insulin. The zinc in the insulin, along with the continuous injections into the sub-cutaneous fat layer leads to this condition which mostly goes undetected.
- Lipohypertrophy leads to reduced or blunted absorption of insulin, thereby leading to high blood glucose levels and long term diabetic complications.



Blunted Insulin delivery

The biggest issue with Lipohypertrophy is **blunted insulin delivery**, which is unexplained high blood glucose levels leading to life-long complications. Studies have shown that these regions can cause an increase in blood glucose levels by about 50-150 points, which raises HbA1C greatly.

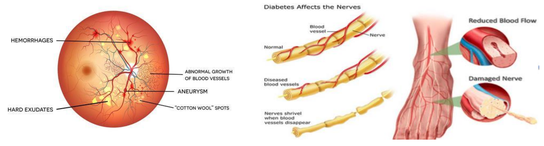
Shown in these images, is the absorption of insulin greatly decreases from the transition from NAT (Normal Adipose Tissue) to LHT (Lipohypertrophy)



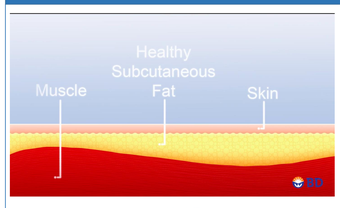
Long-term complications

Lipohypertrophy mostly goes undetected in about 95% of the cases and caused many long term complications of :

- **Diabetic Retinopathy**– development of "micro-aneurisms"
- **Diabetic Neuropathy** – loss of feeling in the fingers or feet
- **Diabetic Nephropathy-** slow deterioration of the kidneys

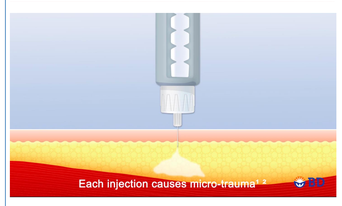


PROGRESSION OF DISEASE



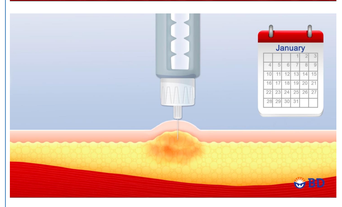
Normal Adipose Tissue

Normal adipose tissue has no inflammation of the sub-cutaneous fat region



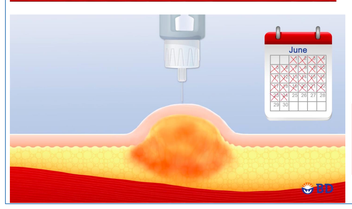
Site of Insulin Injection

Continuous injections of Insulin at the same sites leads to development of excess adipose tissue due to micro-traumas



Undetectable Lipohypertrophy

95% of all Lipohypertrophy is undetectable to the naked eye



Severe Lipohypertrophy

Severe Lipohypertrophy is painful and can take 6 to 12 months to fully heal

CURRENT TREATMENT

The only way to determine Lipohypertrophy regions is very rudimentary where the nurses palpate the areas of injection to detect severely affected regions.

By the time they find out that one has Lipohypertrophy it is often too late and takes 6-12 months to cure these areas.

Site rotation is the only solution to help heal common injection sites, but patients do not know which regions have Lipohypertrophy and can't affectively rotate sites.

FIT Technique Plus* Lipohypertrophy

- Regular site inspection should be a normal part of your injection routine. To check your injection site, feel the area where you normally inject. Look for puffiness, raised areas and redness. Feel for hardness or lumpiness. If it is difficult to see your injection sites, a mirror may help.

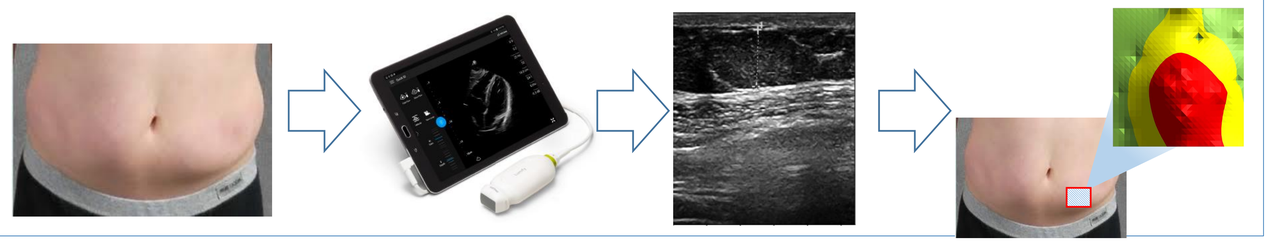
LIPODETECT SOLUTION OVERVIEW

Patient with Lipohypertrophy

Perform **ultrasound scan** of affected region

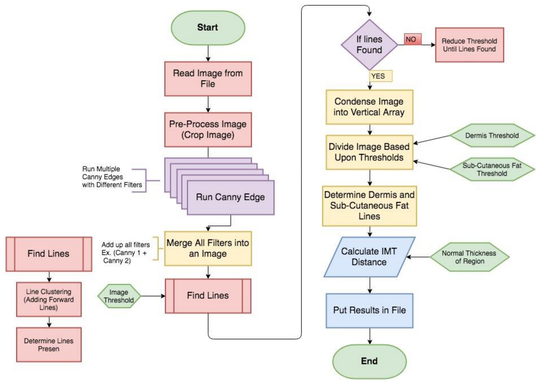
Pre-process collected images

Use **optimized edge detection** algorithms to report results



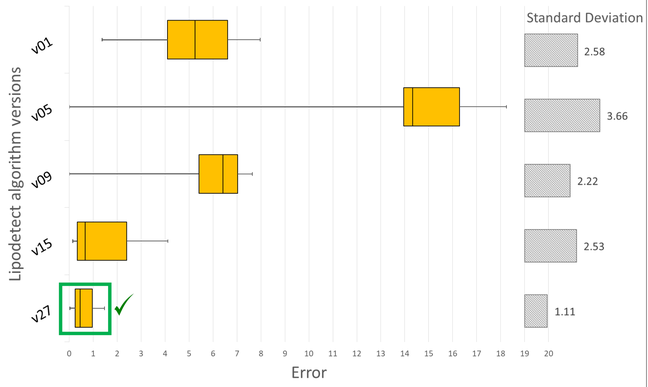
LIPODETECT ALGORITHM

The flowchart below shows the modified edge detection algorithm with matrix calculations to compute the subcutaneous fat of images and detect Lipohypertrophy. This was implemented in Python on Google compute engine



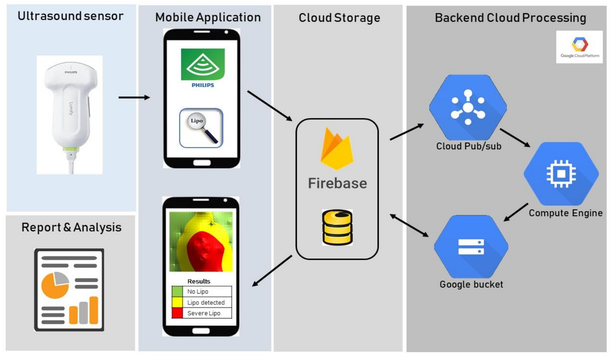
ERROR REDUCTION

The lipodetect algorithm was iteratively improved to reduce error. A total of 27 versions of the algorithm were developed and the final algorithm demonstrated the best results



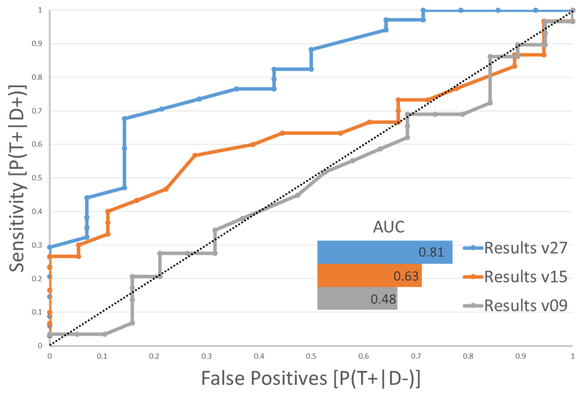
SYSTEM ARCHITECTURE

The detection system consists of a portable ultrasound that connects to a mobile device. The mobile app sends images to the cloud. The backend applications processes the images and sends results to the mobile device. The system is able to scan and detect regions of Lipohypertrophy in real-time



ROC CURVES

The following shows Receiver operator characteristics (ROC) curves of different iterations of the lipodetect algorithm. The final version (v27) shows the highest Area under curve (AUC)



CLINICAL EVALUATION AND RESULTS

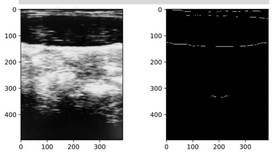
Objectives	Primary – To confirm the applicability of the real-time system to detect Lipohypertrophy Secondary – Understand the development of Lipohypertrophy in multiple patients and provide accurate data on optimal injection locations
Study Hypothesis	The real-time detection system will have diagnosis accuracy and depth detection accuracy of over 85%
Outcome Measures	Primary – Diagnosis of Lipohypertrophy Secondary – Depth of subcutaneous tissue (mm) & proper identification of optimal injection regions
Evaluation of Subjects	10 patients recruited for the study. 5 diabetic and 5 non-diabetic patients
Protocol Summary	1. Images from 4 of the most injected regions were taken (ex. arms, thighs, stomach) 2. The most injected region was analyzed thoroughly and a 5x5cm region was scanned 3. Ground truth distance of subcutaneous region was measured

CONFUSION MATRIX		Target: Positive	Target: Negative
Model	Postitive	81	12
	Negative	5	58
		Sensitivity	*Specificity*
		94%	17%
	Accuracy	89%	
	Error rate	11%	

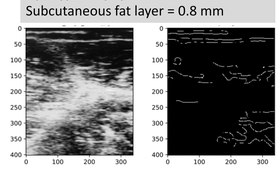
Pilot Study

As a first-step of clinical evaluation, a small pilot study was conducted with two patients. One diabetic and other non-diabetic. The system detected Lipohypertrophy in different regions of the diabetic patient

Patient A – Diabetic
Lipohypertrophy detected
Subcutaneous fat layer = 11.67mm

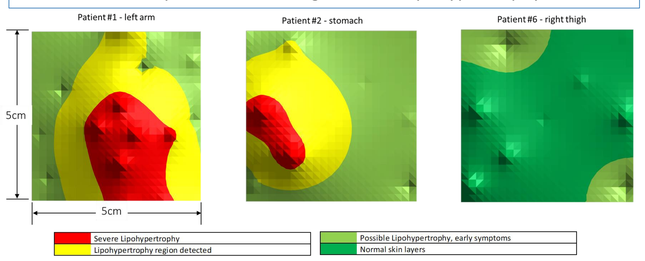


Patient B – Non-diabetic
Lipohypertrophy NOT detected
Subcutaneous fat layer = 0.8 mm



Contour Maps

The system developed generates contour maps of the 5x5cm regions scanned. It clearly identifies the regions with Lipohypertrophy



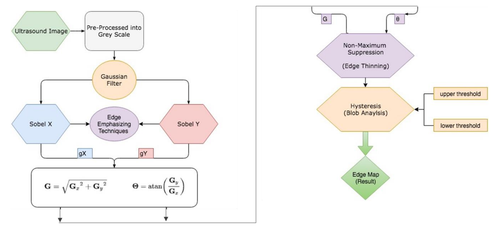
ALGORITHM DEVELOPMENT

The Lipodetect algorithm was built based on a published image dataset from the Profil institute of Metabolic Research, Germany. It is a multi-step process, where the initial algorithm was developed using a single image from the dataset. With an iterative approach, different aspects of the algorithm was fine-tuned to ensure high level accuracy of the algorithm. The algorithm consists of the following parts:

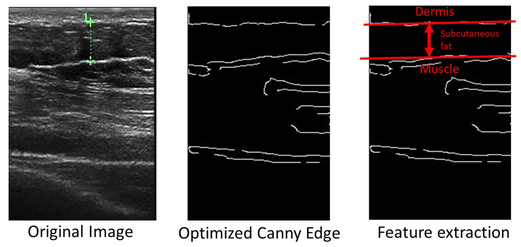
Image Editing: Since the image dataset consisted of varying size of ultrasound images, it was important to pre-process them for a consistent input to the detection algorithm. Parameters from the image like size and ultrasound depth were extracted and provided as inputs for cropping the image to the appropriate size. The editing mechanism was optimized to not lose any useful information of the image.

Edge Detection: This technique uses various mathematical models that aim at identifying points in an image at which the image brightness changes sharply. More than 10 different edge detection techniques were evaluated including Roberts, Sobel, and Canny. The Canny edge detection process is a multi-stage process that resulted in the best detection of inter-muscular lines.

This flowchart shows Canny Edge detection algorithm



Feature Extraction: The edge detection techniques are able to identify multiple lines in the skin layer. The lipodetect algorithm is based on the detection subcutaneous fat layer between the dermis and muscle layer. A critical step in the algorithm is to accurately extract the concerned lines from the images. The best approach was a combination of two ideas, iterative canny edge to brighten the subcutaneous fat layer lines and matrix summation to differentiate the layers. This approach enabled identifying the required features of the image with high degree of accuracy.



Original Image | Optimized Canny Edge | Feature extraction

Classifier: The final step of the algorithm was to develop a robust classifier that is able to utilize the edge detection and feature extraction techniques to predict the presence of Lipohypertrophy.

SYSTEM DEVELOPMENT

Ultrasound Device Evaluation – There were a variety of ultrasound devices that were analyzed through criteria and constraints. Eventually Phillips Lumify Ultrasound device was chosen due to the deployment ability of the code on the final system, along with benefits of portability and cost.

Ultrasound Device	Phillips Lumify	EDAN DUS Portable Ultrasound	SonoSite Portable Ultrasound	Clarius Device	Cardio Tech CT-30 Diagnostic
					
Portable	+	0	+	+	-
Resolution	0	+	-	-	+
Cost	+	-	+	0	-
Deployability	+	-	0	0	-

Mobile App Development – Developed a fully functional android app that incorporates Phillips Lumify that connects to cloud software. This app sends images for processing and retrieves results automatically when processing is done. This user-friendly product is utilized for accurate detection of Lipohypertrophy.

Backend Code – The code implements the lipodetect algorithm in python. When an image is uploaded, the Pub/Sub software triggers the Google Compute Engine to run the algorithm on the image. Once the image is processed the results are placed into a Compute Engine Bucket, which are then be retrieved by the mobile app.

CONCLUSION & FUTURE WORK

The results demonstrate a real-time detection system for automatically detecting Lipohypertrophy in people with insulin dependent diabetes.

As a next step for the project, many more patient images are required to implement machine learning algorithms to further improve accuracy of lipodetect algorithm.

Application of this detection system is feasible in doctor offices as of today. This system can detect and notify patients of optimal injection regions along with undetectable and severe Lipohypertrophy. This can significantly improve the overall HbA1C, thereby reducing diabetes related complication in patients.