Deep Learning based Diagnosis of Muscular Dystrophy in Thigh Muscles

Submitted in partial fulfilment of the requirements for the award of the degree of
BACHELOR OF TECHNOLOGY IN CHEMICAL ENGINEERING

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By

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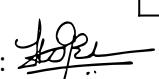
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Acknowledgements

Abstract

Manual diagnosis of neuromuscular illnesses (Muscular Dystrophy) such as muscle dystrophy in the thighs can be a time-consuming and arduous process. This thesis goes into great detail about our work on using deep learning on fat-water decomposition MRI to automate the detection of neuromuscular disorders in the thighs. To aid in diagnosis, a segmentation and classification pipeline was implemented on the MRI picture. The tasks of semantic segmentation and instance segmentation have both been completed.

MyoSegmentum Thighs is the dataset utilised in this procedure. It is made up of 25 MRI scans (3 scans of patients and 21 scans of healthy volunteers).

The U-Net model was utilised for semantic segmentation, whereas ResNet50 was employed for classification. The IOU score was employed as a metric in segmentation, and we were able to get as high as 0.96 IOU-score. We were able to acquire an F1Score of 0.99 for Classification. The Mask-CNN model was utilised for instance segmentation, and we were able to acquire an IOU-Score of 0.92. With appropriate hyper-parameter adjustment, we anticipate that the outcomes can be improved.

As a result, we present our unique segmentation – classification pipeline for clinical diagnosis purposes. AIIMS Delhi is collaborating with us on this project.

Keywords: Deep Learning , Quantitative MRI , Diagnosis, Neuro-muscular disease,Segmentation, Classification, U-Net, ResNet-50 ,Instance Segmentation, Mask-RCNN

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Nomenclature

Symbol	Meaning
NMD	Neuromuscular Disease
ROI	Region of Interest
DMD	Duchenne Muscular Dystrophy
MRI	Magnetic Resonance Imaging
QF	Quadriceps Femoris
GR	Gracilis
SA	Sartorious
HA	Hamstring

1. Introduction

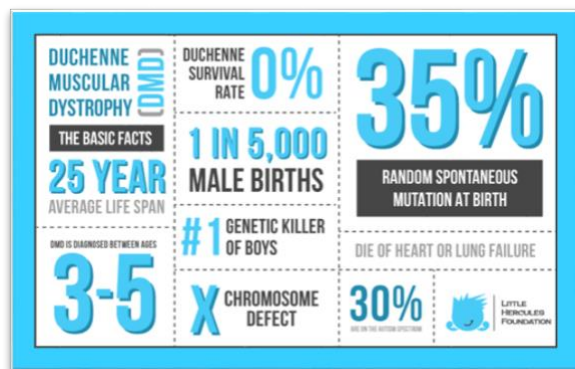Neuromuscular Diseases (NMDs) are the diseases that affect the functioning of the muscles in the body due to glitches in nervous system and muscular system. NMDs form a major class of diseases and can be classified into a number of categories. In this report, we are going to focus on one of the NMD named Duchenne Muscular Dystrophy (DMD). DMD is a rare class of disease. 350 Million people have been reported to be suffering from DMD around the world. In India , only children forms a massive number of 0.8 M to be suffering from DMD. [1]
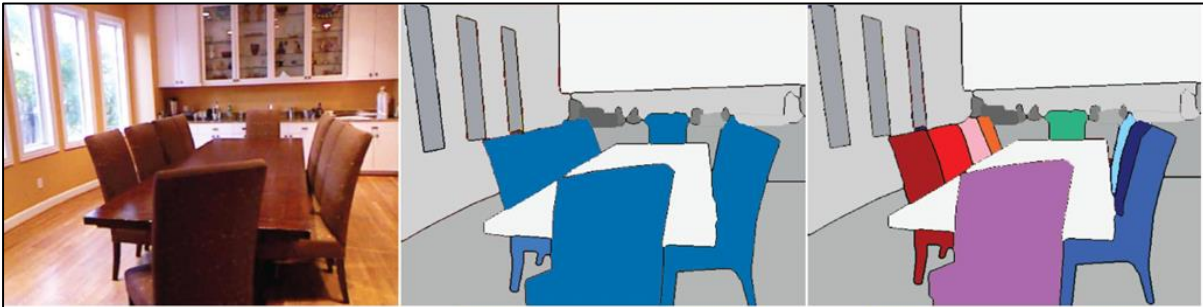
Figure 1   [1]

The reported figures may actually be far less than the actual ones , owing to the fact that its diagnosis of DMD is very much time consuming ,tedious and prone to knowledge of subject matter expert. Also, its invasive diagnosis is very much painful for the patient. DMD is a very deadly disease and its survival rate is also very low. All these facts demands for better and early diagnosis of DMD which is a must pre-requisite for the timed treatment of the patients suffering rom this disease.

Computer vision has recently found a number of applications in the diagnosis of various diseases such as COVID-19, Pneumothorax, and others that can be difficult to diagnose using conventional medical imaging techniques such as magnetic resonance imaging (MRI) and X-rays. Not only has computer vision been successfully implemented, but it has also proven to be quite effective in the detection of various disorders.

As a result, diving into computer vision to solve our problem makes logical. Computer vision, in particular, has only been able to attain such a milestone since the introduction of several deep learning models. As a result, we chose deep learning as a technique for diagnosing NMDs.

In this report, I have focused on specific part of Computer Vision namely Medical Image Segmentation. There may be various kinds of segmentation but we have explored Semantic Segmentation and Instance Segmentation. So it makes a sense for us to dive into what are the differences between them.

Semantic Segmentation and Instance Segmentation

Semantic Segmentation	Instance Segmentation
Semantic Segmentation is the classificaion of pixels in the images to categories of the object.	Instance Segmentation is the classification of pixels in the image to the object instance

The thesis begins with a review of the literature on how this subject has been tackled in the past. This is followed by a full mathematical explanation of the deep learning models employed in this study, such as U-Net and ResNet50. Following that, a thorough explanation of the dataset (Myosegmentum Thighs) was provided. Then, a detailed overview of the applications and libraries that I utilised in my work. Finally, the collected results were discussed, followed by a conclusion, and finally, future work was presented.

2. Literature Review

Problem Statement ; [2]

It has been reported in the literature that DMD is observed to induce fat infiltration in muscles. Fat Infiltration implies unusual increase of fat fraction in muscles. Thus fat-fraction may serves as a better marker in diagnosis of DMD.

Quantitative MRI Analysis ; [3]

In order to estimate fat-fraction, we need to have a effective quantitative MRI technique. To detect the dystrophy using MRI is the key to non-invasiveness in the process. Fat-Water Decomposition MRI is one of the appropriate techniques documented in the literature suitable for purpose of diagnosis. Dixon was the first to develop this technique. It uses chemical shift differences to distinguish MRI signals from water and fat protons, making it excellent for fat-fraction estimation. Multipoint Dixon sequences are now frequently utilised in clinical practise and research to measure intramuscular fat infiltration in the thigh.

Segmentation ; [4]

In thighs, there are namely 4 types of muscles namely Quadradis Femoris, Gracilis, Sartorious and Hamstring, which are prone to fat infiltration so we have to focus on them. Thus it makes sense to segment out those 4 muscles. After getting fat-water decomposition MRI, Segmentation is a critical step for fat-fraction estimate. It greatly limits the use of fat water decomposition MRI for fat fraction calculation because manual muscle segmentation is not only time consuming and complex, but also prone to errors and repeatability issues. According to a study, physically segmenting the four muscle groups of the thighs (QF, GR, SA, and HA) takes roughly 6 hours on average for a scan.

Ding et al. suggested a very novel way of segmenting the regions with the U-Net Model and then distinguishing the normal and abnormal thighs on the basis of mean fat fraction via hypothesis testing to overcome the limitations of manual segmentation.

Using this study as inspiration, we propose a deep learning-based segmentation-classification pipeline for automatically segmenting and diagnosing the NMD from fat-water decomposition MRI. So it's basically divided into two phases: benchmarking and refining U-Net semantic segmentation results, and developing a robust deep learning classification model. Followed by evaluating instance segmentation via Mask-RCNN model built in Detectron2 library, with the aim of better segmentation and focus on individual muscles for better diagnosis.
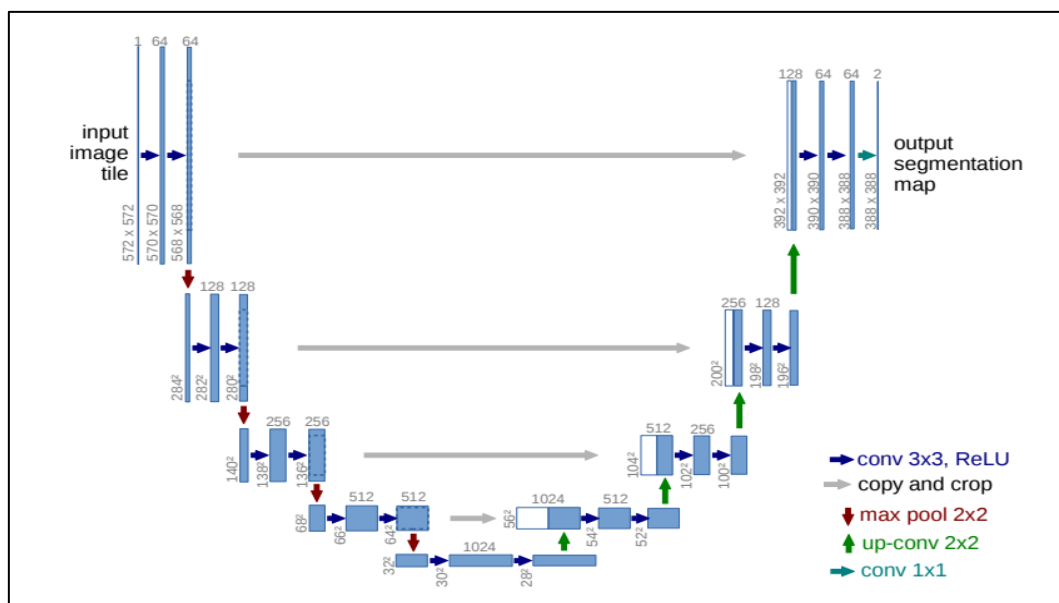
U-Net ; [6]

Figure 2

U-Net was first invented by Olaf Ronneberger et al. for Biomedical Image Segmentation in 2015. It was proven to be a breakthrough for segmentation purposes even with smaller set of data.

U-Net is a fully Convolutional Network (FCN) .It consists of following components :

- Encoder :
  It is the contraction path and captures context in the image, for the required segmented object. Encoder is basically a stack of convolution layers and activation functions. It can also be any standard architecture. In our case, we have used "ResNet34" as the encoder for U-Net Model.
- Decoder :
  It is the expanding path , to achieve localization of context in the image. It basically consists of transposed convolution operations.
- Skip Connections :
  These are the mathematical constructs that connect the outputs of constituent convolutions in encoder to corresponding transposed convolution in the decoder

We chose U-Net for segmentation because:

i)   It can handle high-resolution images (672*672) in our case.
ii)   For benchmarking purposes.
iii) It is known to have won a number of segmentation competitions and to be particularly good at segmenting biomedical images.

ResNet ; [5]

ResNets are deep residual networks that were developed in 2012 by Kaming He et al.[6]. They were a game-changing invention in the field of computer vision since they enabled for more efficient and accurate training of deeper networks.

Figure 3

They are based on the simple fact that identity matrices can be layered on top of each other, allowing only the residual to b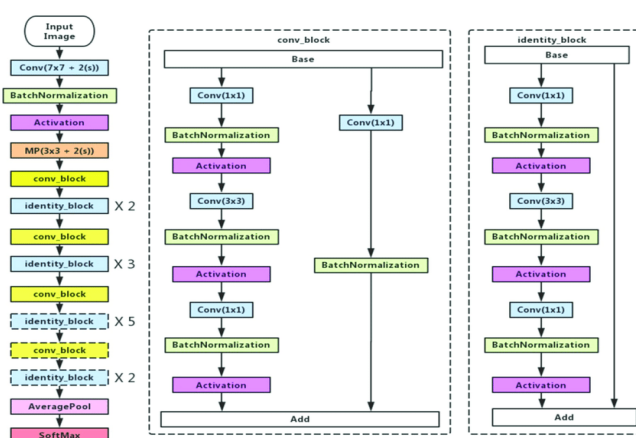e trained rather than the entire function, which can lead to vanishing and exploding gradients. To take this difficulty into account and solve it efficiently, they used the skip connections as indicated in the diagram.

This is referred to as "Identity Skip Connections" in the industry. The introduction of these skip connections allows the network to be efficiently trained, as seen by the fact that training error lowers as the network becomes more complex.

However, if we choose to have a higher number of layers, we risk overfitting. Various layers can be assigned to have any number of layers, for example, ResNet34 has 34 layers, ResNet50 has 50 layers, and so on.

Now, we've decided to employ ResNet34 as the backbone of the UNet Model because it's well known that deeper networks, as in the case of the U-Net encoder, produce the greatest results.

We utilised the ResNet50 model to classify healthy and sick patients because it has previously won classification competitions.

Mask - RCNN; [7]

Facebook's Mask RCNN architecture is a combination of two architectures that enables for object instance segmentation. Object detection and semantic
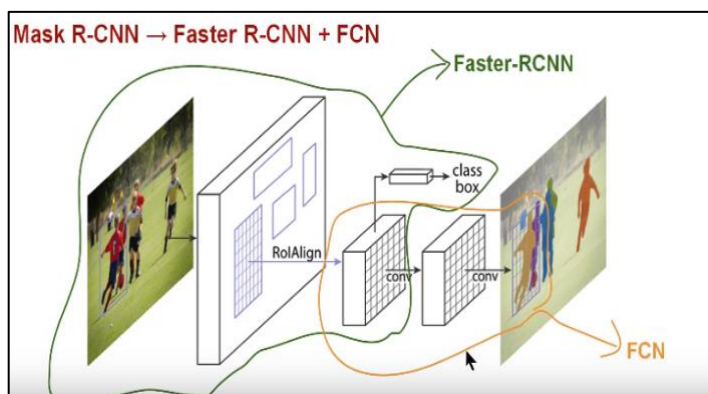
Figure 4

segmentation are combined in this method. The first component is the Faster R-CNN, and the second is the Fully Convolutional Network. The state-of-the-art object detection architecture, Faster R-CNN, was introduced as an upgrade to R-CNN and Fast R-CNN in 2016.

Faster R-CNN has an extension called Mask R-CNN. A third approach is described, which uses classification and bounding box regression to predict segmentation masks for ROIs. The mask branch is a pixel-by-pixel segmentation mask prediction FCN that is applied to each ROI[5].

Figure 5

The bounding boxes, class labels, and masks of ROIs are typical outputs from this model; however, for our use case, it is the masks that are most important, as we need to distinguish our ROIs from each other and the backdrop.

In detection and segmentation tasks, Mask R-CNN has the benefit of using Faster R-CNN, which

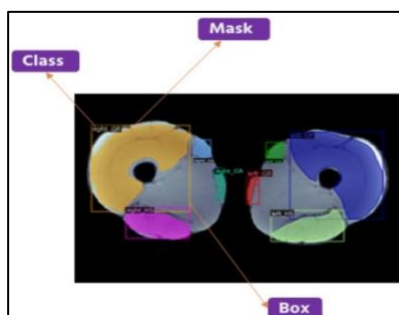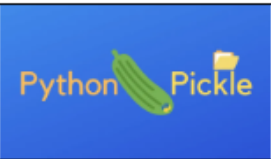includes the RoI Align, a feature extractor from our ROIs. This is an improvement over the previous method of RoI pooling, which was based on a rigid quantification methodology. Extracted features can be better aligned with the input using RoI align. It also ensures that the spatial orientation of features is maintained, preventing data loss.

If we combine the left and right thigh MRIs, we get a total of eight incidences per picture, four from the left and four from the right. The masks are symmetrical to a high degree. The muscle locations on the left and right thighs aren't perfectly symmetrical in reality.

3. Description of Software and Procedure

3.1   **Softwares Used**[8]

S. No.	Software/library Logo	Software/library Name	Brief Description
1	python	Python 3	Python 3 is a programming language, it have excellent collection of various libraries that makes is it very much suitable for machine learning projects. It have libraries like numpy, pandas , matplotlib etc
2	OPTUNA	Optuna	A Powerful Python Library for hyper-parameter optimization based on Bayesian Optimization
3	NVIDIA QUADRO	GPU	Graphic processing unit(GPU) allows to process the image faster and it is very much popular in the field of computer vision. We are using 2 NVIDIA Quadro GPU, with 16 GB each.
4	python MedPy	MedPy	MedPy is an image processing library and collection of scripts targeted towards medical (i.e. high dimensional) image processing
5	Python Pickle	Pickle	Python pickle module is used for serializing and de-serializing a Python object structure
6	Segmentation Models	Segmentation_Models	Python library with Neural Network Architecture for Image Segmentation based on Pytorch
7		Pytorch Lightning	A lightweight pytorch wrapper for training, validating and testing maching learning and deep learning models

3.2 Pipeline
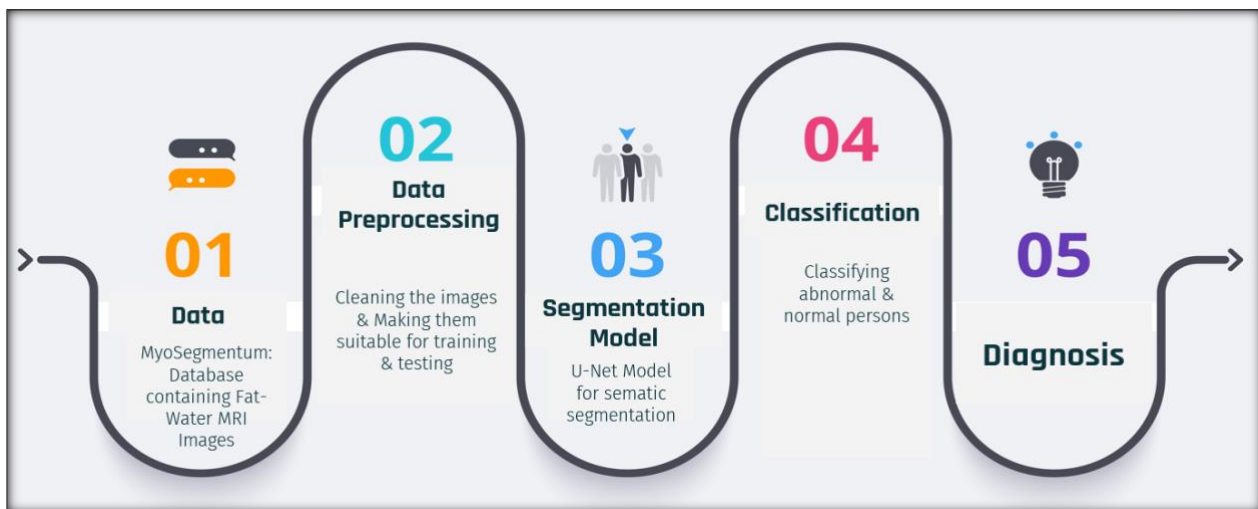
Figure 6

This section discusses the deep learning pipeline that has been proposed for diagnosing NMDs. The core concept behind this innovative pipeline is segmentation followed by classification. In laymen's terms, the technique is as follows:

1. The pipeline receives fat-water decomposition MRI as an input.

2. The data is then cleaned and pre-processed to make it acceptable for segmentation.

3. The ROIs (muscle areas) necessary for classification are delineated by the Segmentation Model (U-Net).

4. The ResNet50 Model is used to classify the masks acquired by the Segmentation Model.

5. Our model's inferences and expert's advice will be used to make a final diagnosis.

Dataset[9]

The use of magnetic resonance imaging (MRI) can aid in the evaluation of muscle structure as well as the diagnosis of a variety of illnesses and neuromuscular diseases. Quantitative MRIs with chemical shift encoding fat-water images can also be used to quantify muscle volume and fat fraction.
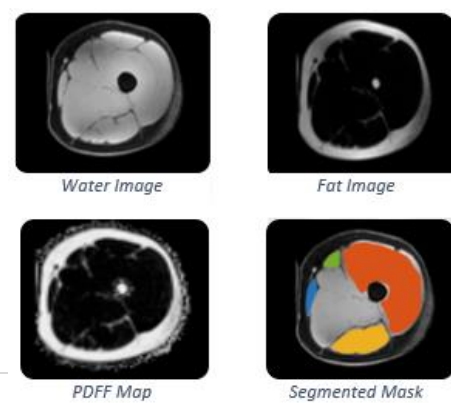
MyoSegmenTUM thigh is the dataset we used for our thesis. This includes 15 healthy individuals and four patients with NMD who had MRI pictures of their left and right thighs with a voxel size of 3.2x2x4 mm3[7]. The dataset contains PDFF maps, fat images, and water images of the thigh area, and the file formats in the dataset are ".dcm" and ".nii." We used ".dcm" files for our model's training and testing. The quadriceps femoris muscle, sartorius muscle, gracilis muscle, and hamstring muscles have been manually segmented and supplied in ".mha" format. The data provided is volumetric, and we used 2D slices to do our research. This dataset was created specifically to aid research in the area of automatic muscle segmentation.

The tables below explain the characteristics of healthy and unwell patients:

SUBJECT ID	GENDER	AGE	WEIGHT [KG]	HEIGHT [CM]	R_QF_STRENGTH MEASUREMENT 60˚ [NM]	R_QF_STRENGTH MEASUREMENT 90˚ [NM]	L_QF_STRENGTH MEASUREMENT 60˚ [NM]
HV001	m	30	99	179	369	323	
HV002	m	25	103	191	372	231	
HV003	m	21	96	186	336	270	
HV004	m	32	88	177	276	204	
HV005	m	48	89	192	245	183	
HV006	m	26	90	180	321	204	
HV007	m	22	64	174	246	157	
HV008	m	25	86	189	316	225	
HV009	m	27	85	182	282	224	
HV010	f	24	69	169	220	120	
HV011	m	20	115	177	218	202	
HV012	f	39	72	164	210		159
HV013	f	25	76	170	176		187
HV014	m	31	87	189	233		216
HV015	m	41	77	174	237		228

https://doi.org/10.1371/journal.pone.0198200.t001

Figure 7

SUBJECT ID	GENDER	AGE	WEIGHT [KG]	HEIGHT [CM]	DISEASE	MRCSCORE_R_KNEE_FLEXION	MRCSCORE_L_KNEE_FLEXION	MRCSCORE_R_KNEE_EXTENSION	MRCSCORE_L_KNEE_EXTENSION
P001	m	52	95	181	DM2	5/5	5/5	5/5	5/5
P002	f	52	79	168	LGMD2A	4/5	4/5	5/5	5/5
P003	m	41	98	191	ALS	5/5	5/5	4/5	5-/5
P004	f	66	90	165	DM2	5/5	5/5	5/5	5/5

https://doi.org/10.1371/journal.pone.0198200.t002

Figure 8

Data Pre-Processing

| Input Image | Remove Subcutaneous fat via Thresholding | Remove Skin Via Ordered Statistic filtering i.e. Median Filter | The obtained mask was put on the Fat map to get the required |
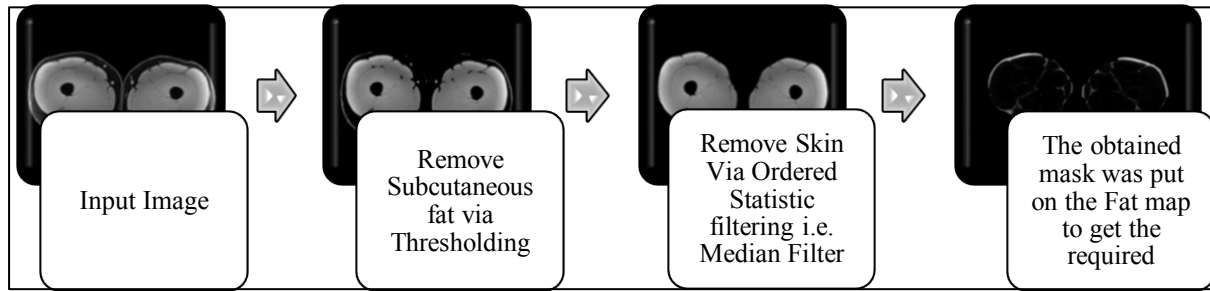
The image pre-processing was done mainly on water images:

Thresholding: [10]

It's one of the simplest ways to digitally segment and process photos. A grayscale image is turned into a binary image (i.e., an image with only black and white pixels) in this method[8]. In thresholding, a specific threshold intensity, say T, is chosen, and the picture has varying intensities throughout the space, say I at a specific position (xi, yj). If I is greater than T, the pixel is assigned a white colour, otherwise it is assigned a black colour.

We used our data to eliminate the subcutaneous fat, which is the additional fat that exists between the skin and the thigh region.

Ordered Statistic Filtering: [11]

It is the mathematical technique by which a non-linear spatial filter replaces the value in the centre pixel with the value derived from the ordering of pixels in the filter's image region. In our example, we utilised a median filter, which replaces pixel values with the median of pixel values in their immediate vicinity. [9] For image processing, median filtering is the most prevalent method.

We used the Median filter to eliminate the skin region from our data. For the Fat images following pre-processing was done:

Masking:

Only the indices for the water picture that were not black were extracted in this method, and these indices were then extracted for the fat image, making fat image pre-processing faster and more in line with water image pre-processing.

For the pre-processing of mask images , the following step was done:

Note: The following preprocessing of mask images was done for Semantic Segmentation only. For Instance segmentation, all the masks were taken separately.
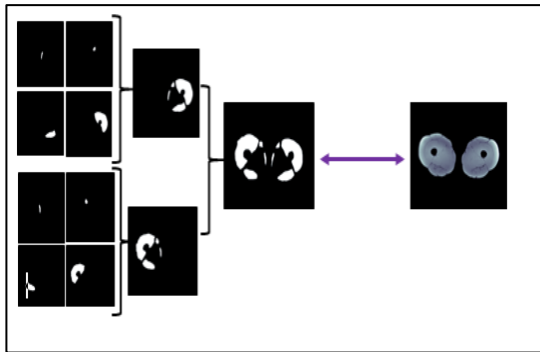
Combination:

Figure 9

Masks of four muscles, QF, GR, HA, and SA, are included for both the left and right thighs in the dataset MyoSegmentum. So, using a self-written Python script, we merged all of the different muscles and created a mask. The illustration beside shows how it was done.

All images were pre-processed using a python script, and the pre-processed images were saved in a separate folder in pickle format so that they could be conveniently retrieved during deep learning model training.

Segmentation Models

Semantic Segmentation

U-Net is utilised to execute the delineation of four ROIs, namely QF, GR, HA, and SA, as mentioned in the preceding section. Now, both the water and fat images should be important for segmentation, so we stacked them on top of each other and created training and testing data in various ratios.

For the implementation of U-Net, we used the Segmentation Models Pytorrch package and ResNet34 as the backbone.Further for the training purpose , Pytorch Lightning Framework was used for effective and trivial wrappers provided by it The accuracy of segmentation was measured using the IOU-score. In a nutshell, the IOU-score is the ratio of the overlapping area of a segmented mask to the union of the predicted and actual mask areas.
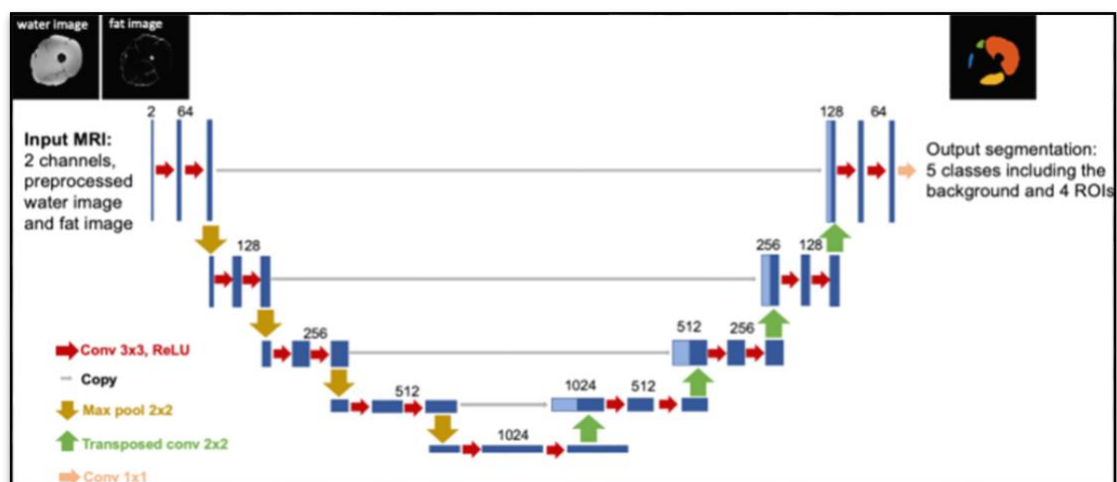

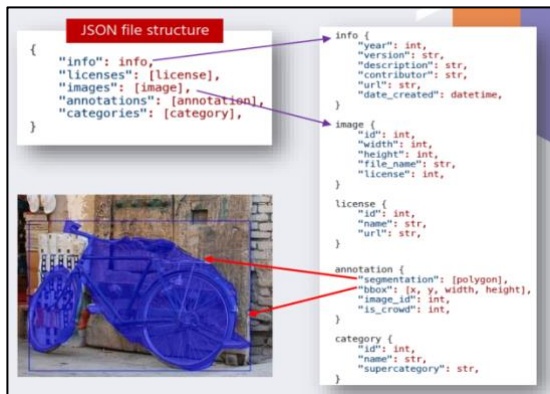*Figure 10*

Instance Segmentation

Figure 11

For Instance Segmentation, Mask-RCNN model is used. It has been described in detail in Literature Review Section. Now , here we describe the process that we used for its implementation. I have used Mask R-CNN model from the Detectron2 library and converted the data to COCO format in order to carry out the work.

COCO stands for Common Objects in Context and is one of the most widely used picture segmentation, captioning, and object detection datasets. It's generally used for creating bespoke segmentation and object detection datasets, and our Detectron2 model Mask R-CNN only takes datasets in this format. The picture information, the coordinates of an arbitrary polygon surrounding the object of interest in the image, and the bounding box coordinates are all contained in the COCO file format[6].

There are a multitude of softwares and tools available for creating one's own custom dataset in COCO file format, including VGG annotator and labelMe. Only the coordinates of the polygons containing the ROIs present in the masks had to be extracted because the working dataset already had the binary masks. Since, OpenCV includes an integrated function for extracting contours, it was employed to complete this challenge. These are also known as annotations since they are utilised to quantify the demarcation of all the different ROIs' boundaries.

Classification model

The categorization was conducted out using the water MRI Images masked by annotated masks, which were labelled as healthy or unhealthy, and a target set was formed as a result. Although it is self-evident that classification must be done for a person, we chose this path because the data we had was limited and we lacked the resources to train on 3D data. Instead, we will input all of the 2D slices of the masked water images separately and predict whether they are healthy or unhealthy slices. Now, let's say we have 65 slices[10] of masked water MRI images, and we want to forecast if each slice is healthy or unhealthy. We'll set a threshold of T, and let's say we anticipate H healthy slices out of 65 and if H>T , then the patient is healthy and vice versa.The following schematic shows how our model works
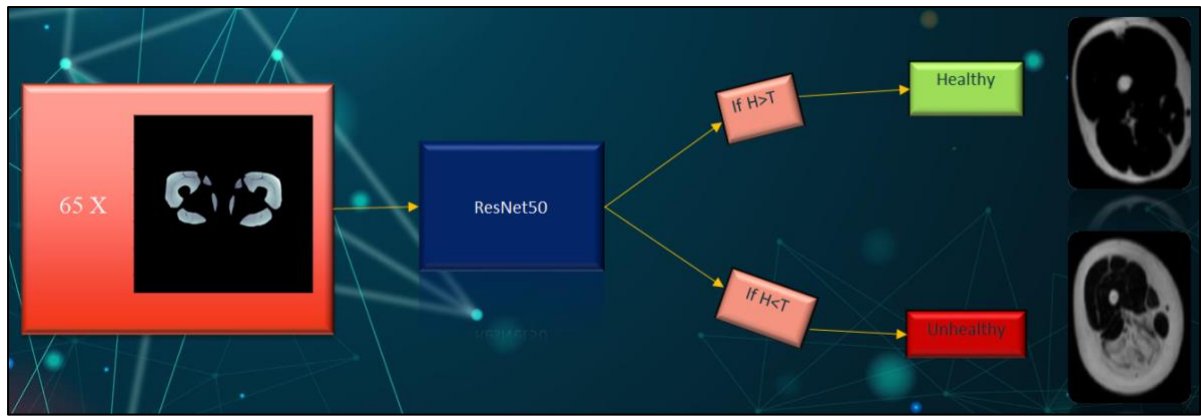
Figure 12

The classification of 2D images was done with ResNet50, and the rest was done with a simple Python script.

4. Results and Discussion

Semantic Segmentation

For the semantic segmentation, U-Net model is used. For the input, water and fat images were stacked and so 2 channel input image (672*672 pixel^2) was put in the model and The hyper-parameters used for the model were chosen to be learning rate and batch-size. The learning rate was varied between 10^(-1) and 10^(-6) . And batch-size was varied between 4 and 20. For Hyper-parameter Optimization, a library called "Optuna" was used which is based on Bayesian optimization. Based on this , 10 trials were done on 50 epochs. The best IOU-Score came out to be .96844 at learning rate of .02678 and batch size of 17 was used. For training purpose 16 GB Quadro GPU was used.

Qualitative Analysis of Results

The graphics below provide a qualitative representation of our predictions based on previously uncovered data. There is a strong resemblance between the expected and actual masks. And it clearly establishes U-credibility Net's in doing automatic segmentation for biomedical images.
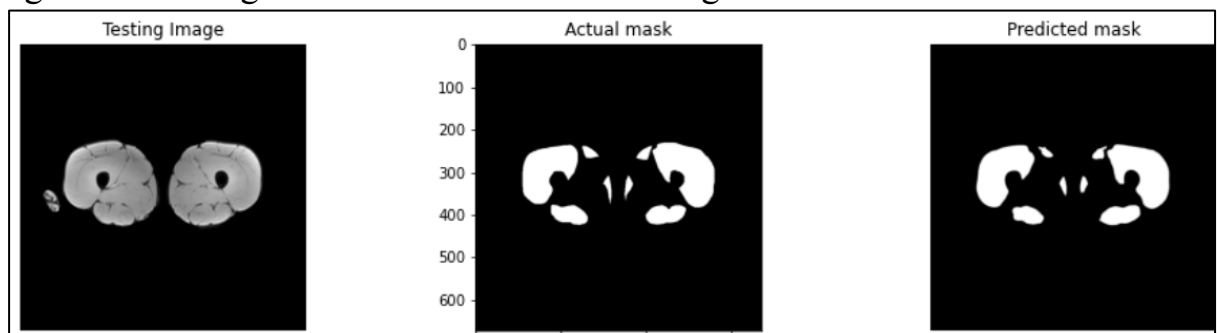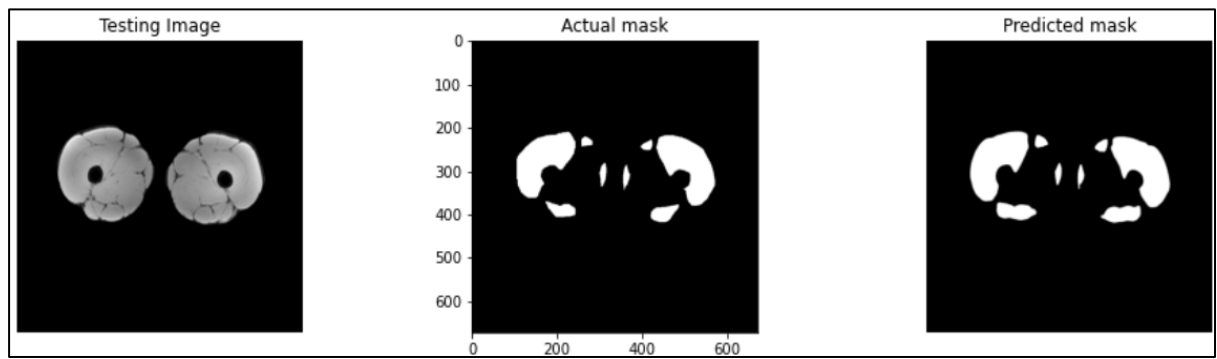
Figure 13

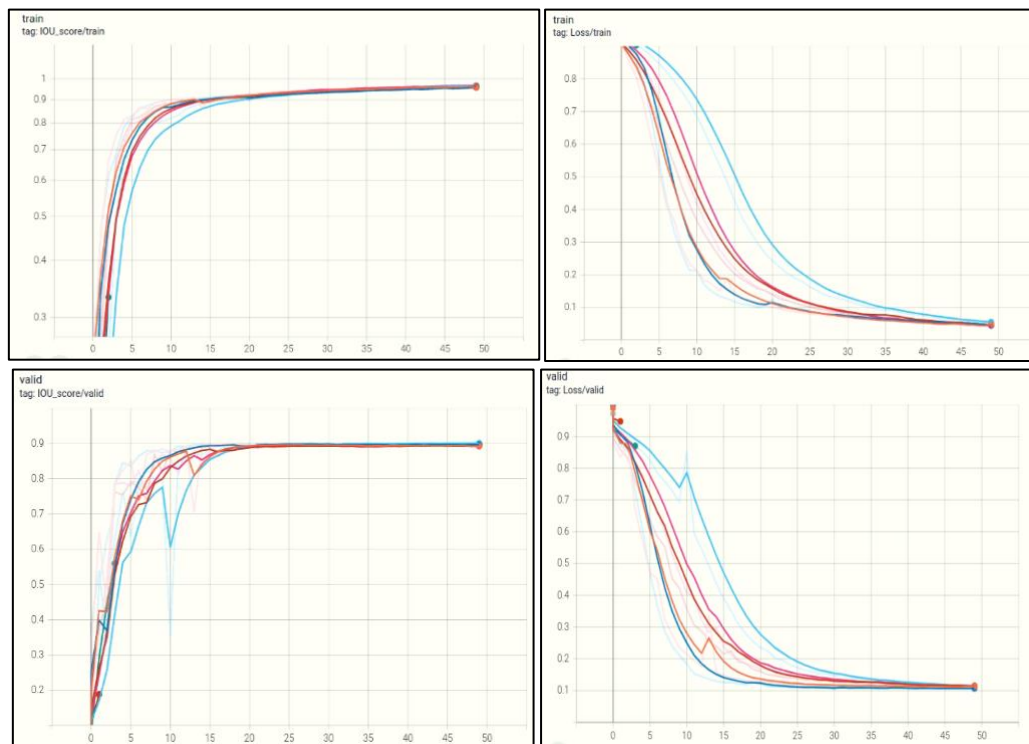## Quantitative Analysis of Results

Figure 14

The above graphs shows loss and IOU-Score v/s no. of epochs for training and validation dataset, for the 10 trials in the hyper-parameter optimization. We were able to achieve a IOU-Score of .964 which is quite higher than reported in literature of .92. Hence we can say that we have carried out semantic segmentation successfully.

Instance Segmentation

For the instance segmentation ,Mask-RCNN model is used. For the input , water MRI images (672 * 672 pixel ^2)was put in the model . Currently, the learning

rate is taken to be 5e-4. An exceptional score of IOU-Score of .92 was obtained on stack of 6 Healthy Volunteers and 3 Patients. Hyper-parameter optimization is yet to be done for more better results for instance segmentation.

Qualitative Analysis of Results

I tested the trained Mask-RCNN model, on unseen images. Striking similarity can be seen between the predicted masks and actual masks in the following figures:
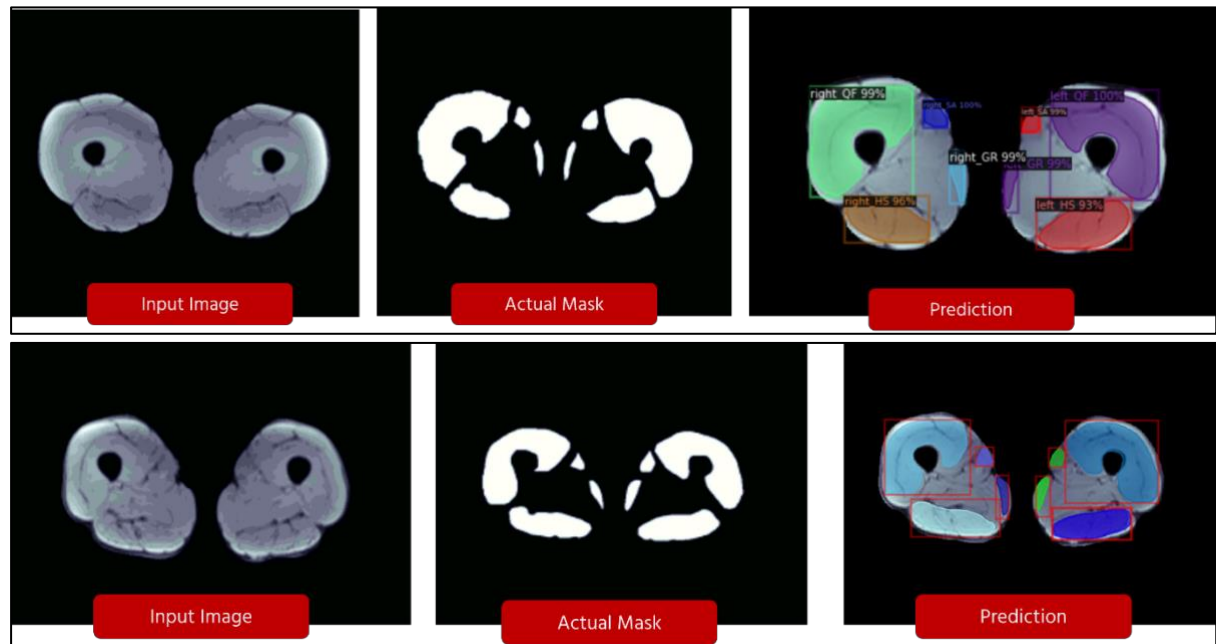

Figure 15

Quantitative Analysis of Results

The learning curves of training were made i.e. IOU-Score and total loss were plotted with steps as shown in the figure shown below:
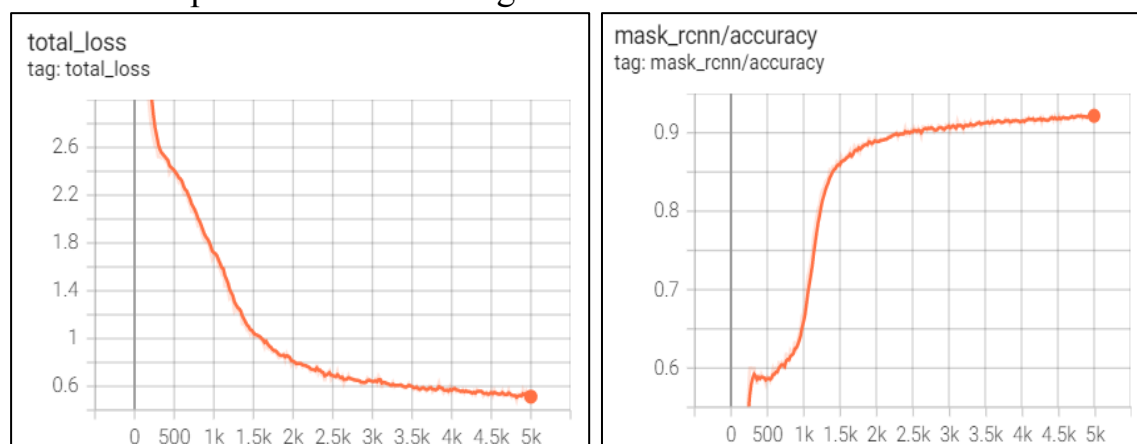

Figure 16

Classification

For classification, we used ResNet50 model. The input images were masked water MRI of shape 672*672 pixel^2. Learning rate and batch size were specified as hyper-parameters for the model. The rate of learning was varied between 10(-1) and 10(-6). The batch size ranged from 4 to 20. A Python library "Optuna" which is based on Bayesian optimization, was used for Hyper-parameter Optimization. 10 trials were run on 50 epochs based on this. The model was able to achieve the accuracy and F1-Score of as high as .99 with a learning rate of .05678 and a batch size of 15. A 16 GB Quadro GPU was used for training.

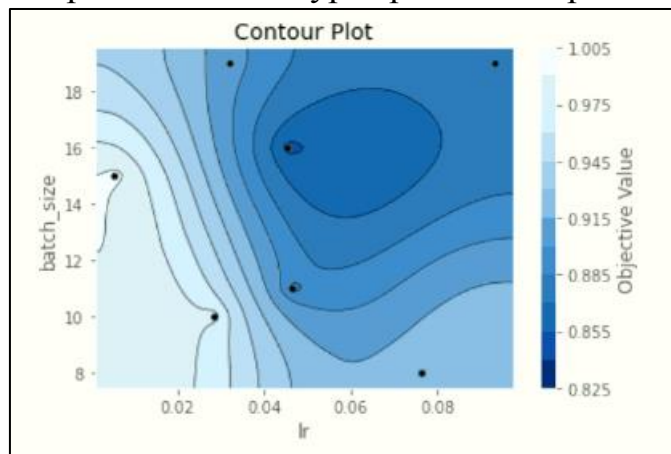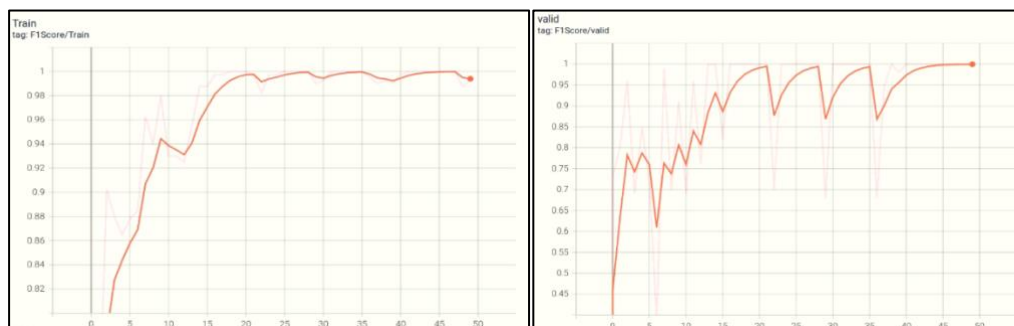The following contour plot shows the hyper-parameter optimization results.

Figure 17

The learning curves were also made, here F1-Score and Loss v/s no. of epochs have been shown for the best trial.
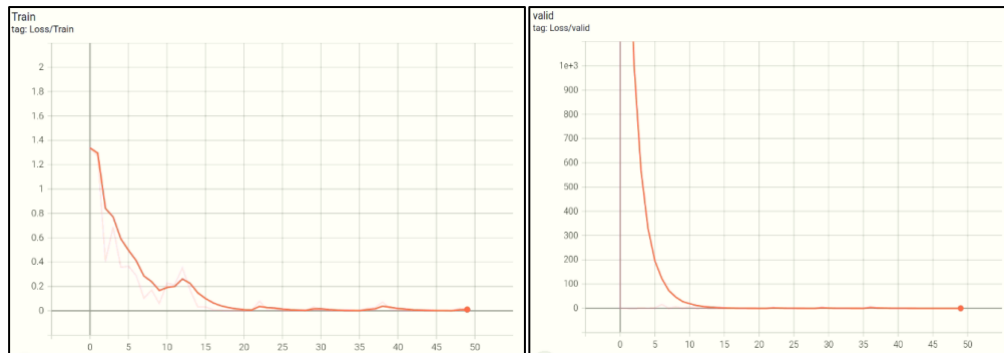
Thresholding:

Here we describe thresholding as the process to find a threshold T such that for any given stack , if we predict H% healthy images then H>T makes the stack healthy and vice versa. So we adopted hit and trial method in order to find the required threshold. We found that the threshold should be 10%. Such a low value of threshold is attributed to the large no. of False Negatives. More introspection needs to be done in this case.

5. Conclusion

We were able to design a system for automated diagnosis of NMDs using our unique pipeline, which comprises segmentation and classification (particularly muscular dystrophies). It has the clear advantage of very smooth and efficient automated segmentation(both semantic and instance segmentation), which takes only around 10 seconds to delineate ROIs, compared to roughly 6 hours for manual segmentation. It can also be inferred that instance segmentation can provide us with more detailed and precise muscle that has been affected.In contrast to invasive treatments like biopsy, which is a painful and time-consuming process, it also provides a non-invasive strategy for diagnosing muscular dystrophy.

6. Future Work

AIIMS Dataset

MRI images can be collected for various individuals with NMD because this initiative is in conjunction with AIIMS, which will make our model more generalisable in the future. We have submitted a joint proposal for the same's ethical clearance.

End to End Software

A full-fledged software can be created with a graphical user interface so that non-technical people can benefit from our efforts. A software that provides

automated diagnosis based on cutting-edge technology such as deep learning has a lot of room in the medical sector

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