Tech Review for Rheumatoid Arthritis Mobile App

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Abstract

This document outlines some of the frameworks, software paradigms, and data collection methods that Group 5 will use in the process of creating our application to measure rheumatoid arthritis. I will begin with a broad overview of why we made our current design choices, how that drives the need for data collection, and the various technologies that we considered for each part of our software. Finally, I will end with an explanation of our data collection techniques.

I. The State of Rheumatoid Arthritis Treatment

We are attempting to improve conditions for patients living with Rheumatoid Arthritis. We chose to focus on this particular disease because the company we are working with already does work to serve people with the condition. We chose to create software to address the problem because we are required to for our senior project and because, as computer science majors, we have more experience writing software than creating drugs or identifying blood-based biomarkers that correlate with Rheumatoid Arthritis activity. In order to determine where software could make an improvement in the treatment of Rheumatoid Arthritis, I believe it is helpful to examine how the disease is currently treated, and look at research to determine the areas in which new or better software might create better outcomes.

People suffering from Rheumatoid Arthritis have experienced significantly better outcomes over the last 20 years thanks in large part to the use of disease modifying drug therapies such as sulfasalazine and methotrexate. James Gwinnutt, an author of a study that examined the relationship between use of these disease modifying drugs and patient disability said, "People living with Rheumatoid Arthritis have experienced significant improvements in their daily lives which is probably down to early and more aggressive treatment of the disease, according to new research from The Universities of Manchester and East Anglia." Gwinnutt also said, "In the early 1990s early intervention would happen in about 30% of cases. Nowadays, that figure is probably more like 60-70%. There's no reason why this improvement could not extend further."[1]

In another article from the Arthritis Foundation, Dr. Stephen Paget, a rheumatologist and physician-in-chief at the Hospital for Special Surgery in New York City exlained, "I think it's pretty clear right now that if a patient has antibodies to rheumatoid factor (RF) or cyclic citrullinated proteins (anti-CCP) at any time during the course of disease – from day one to 12 weeks or 12 years – then he has a greater risk for persistent disease that is worse and more destructive. Those patients need aggressive therapy that's constantly monitored."[2]

II. Our Approach

Raising the percentage of early interventions by creating more convenient and cheaper ways of monitoring the disease is where we believe software can make a contribution. Software has a unique advantage over blood tests and doctors office visits when it comes to monitoring disease activity: the marginal cost of producing one more copy is pennies, and it requires no specialized hardware, testing facilities, or trained personnel. If one accepts these premises as true, then the remaining question is: what type of software is best suited for monitoring Rheumatoid Arthritis?

To answer this, one must first answer the question: what is Rheumatoid Arthritis and what are the markers of disease activity? RA is first and foremost an autoimmune disease, so any measurement we use to infer disease activity must be highly correlated with underlying immune system activity. There is no single gold standard measurement of RA activity. Instead, most clinical trials use a variety of measurements including blood tests, tender joint counts, swollen joint counts, patient self-reporting, erythrocyte sedimentation rates, radiography images, and others.[3]

We believe that clinically significant markers of disease activity should also show up in images. Immune system activity is visible in the hands of patients with RA during periods of high disease activity such as flares. Widespread adoption of cell phones with high quality cameras and a means of downloading software means that a great way of delivering this solution to people is via a phone app. Our solution is to make an app that uses the phone's camera to take a picture of the hands of people with rheumatoid arthritis and uses software to measure signs of disease activity present in the picture.

Fig. 1. A comparison of a normal hand (left) vs a hand undergoing a rheumatoid arthritis flare (right)

Given an image and the right piece of software, it should be possible to extract the information present in the image to create a measurement of underlying disease activity. The question is what type of software is appropriate for the task?

III. Selecting a Software Paradigm to Analyze Images

Successful applications of machine vision started showing up in niche areas as early as the 90's. In 1991, the ability to recognize handwritten letters and numbers and translate them into standard ASCII characters of a particular font was already showing up in consumer products such as the PenPoint Operating System. [4] Business applications of machine vision continued to mature and improve throughout the 90's and early 2000's. But one area that was still mostly beyond the reach of computers was the ability to classify and localize complex objects within a single image.

Progress in this area took a dramatic leap forward in 2012 when a deep learning neural network named "Alex Net" took first place in the ImageNet object recognition contest. It won the competition handily, achieving 84.5% accuracy with the closest competitor, a linear classifier, coming in at 73.8%. Every winner of major image recognition competitions since then has been some type of deep convolutional neural network. This begs the question: is a deep learning convolutional neural network the obvious choice for measuring rheumatoid arthritis in images? The answer is yes. But before I move on to addressing the implications of using a convolutional neural network, let me explain why the other choices are poor.

A. Support Vector Machines

Before deep learning neural networks were shown to be a viable competitor in the area of machine vision, we had support vector machines and linear classifiers. A support vector machine represents features in an image as components of an N-dimensional vector. It then uses the labels for each image to try to construct a hyperplane that most cleanly divides the data into its appropriate groups.

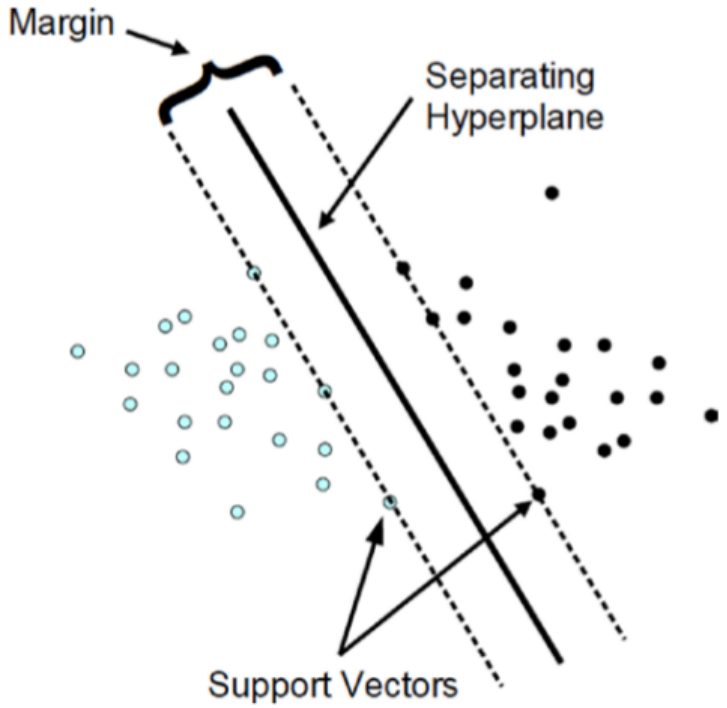

Fig. 2. A simplified diagram showing how a support vector machine categorizes images using hyperplanes

We could try to use a support vector machine to analyze rheumatoid arthritis activity. But support vector machines achieve lower accuracy on almost every image-related task. So that wouldn't make much sense.

B. Human Experts

Another alternative would be to use the app to connect a patient with a human expert with experience diagnosing rheumatoid arthritis. We think this too would be a poor alternative. The human expert would be signficantly more costly, feedback would not be immediate, our product's growth would be limited by the number of RA experts we could get to participate, and our best case outcome would be to involve a large number of highly trained experts in hours of mind-numbing image classification. Another issue would be the difficulty of recruiting those doctors, arranging payments to them for their services, and convincing patients or insurance companies that our product had a big enough effect on outcomes to justify the increased expense. Such a roadmap would be akin to making a remote doctor's visit app. Such technology would no doubt have its use, especially for customers in sparsely populated areas where a trip to the doctor takes a long time, or those in countries with few doctors. But it would not be the most suitable solution to the specific problem we are trying to solve.

C. Convolutional Neural Networks

So a convolutional neural network is our software paradigm of choice. Convolutional Neural Networks have a tremendous cost advantage over humans and an accuracy advantage over support vector machines. Their ability to automatically extract features from an image and use them to categorize or otherwise analyze images gives them a clear advantage over much simpler support vector machines. Programming such a piece of software, troubleshooting it, and getting experience with modern tools used in the business world such as TensorFlow will also have lasting benefits for the members of our group as we transition from school to the work place. There are a number of technical choices implicative in our decision which I will now address.

IV. Creating a data collection tool

There is a reason no one has made a neural network to measure RA activity before now: neural networks need thousands of images to classify objects with high accuracy. The image database to train our proposed network simply doesn't exist yet. And to create it, one must have a method of collecting thousands of images from the hands of hundreds of people, all of whom have rheumatoid arthritis, and all of whom are willing to take an accompanying survey, the results of which will be used to label the images. These labels are crucial for training: they are the supervision in supervised learning. Collecting these images will be difficult and expensive. Thankfully Karate Health has agreed to fund collection of several thousand of these images, provided we create the tools to collect them. This is the first technical hurdle that must be overcome.

We want our application to work on Android and iOS on a wide variety of devices with different phone cameras, in different lighting conditions. To achieve this performance, we need a data set that contains images taken in many different lighting conditions using many different cameras. This means we will need to create a phone app for Android and iOS that gives simple instructions to users about how to take pictures of their hands. We will then have to convince hundreds of people with RA to download this app, sign a digital consent form agreeing to let their data be used for this project, take pictures of their hands, and fill out a corresponding survey answering questions about the current state of their disease. There are three choices for how to develop this data collection tool: make it using Xamarin, make a progressive web app, or make a separate app for both Android and iOS.

A. Developing a separate data collection app for iOS and Android

This path is essentially the backup backup plan. If niether Xamarin nor progressive web apps turn out to be a viable means of making the data collection tool, we can always fall back on making an app for each operating system. Obviously we don't want to do this because it will mean either twice the amount of work or that our app will only be available for a single operating system.

B. Progressive Web Apps

Progressive web apps (PWAs) are interesting because they allow for a regular mobile website to incorporate some of the features of an app like push notifications, pin to home screen, camera access, and a host of other features.[5]

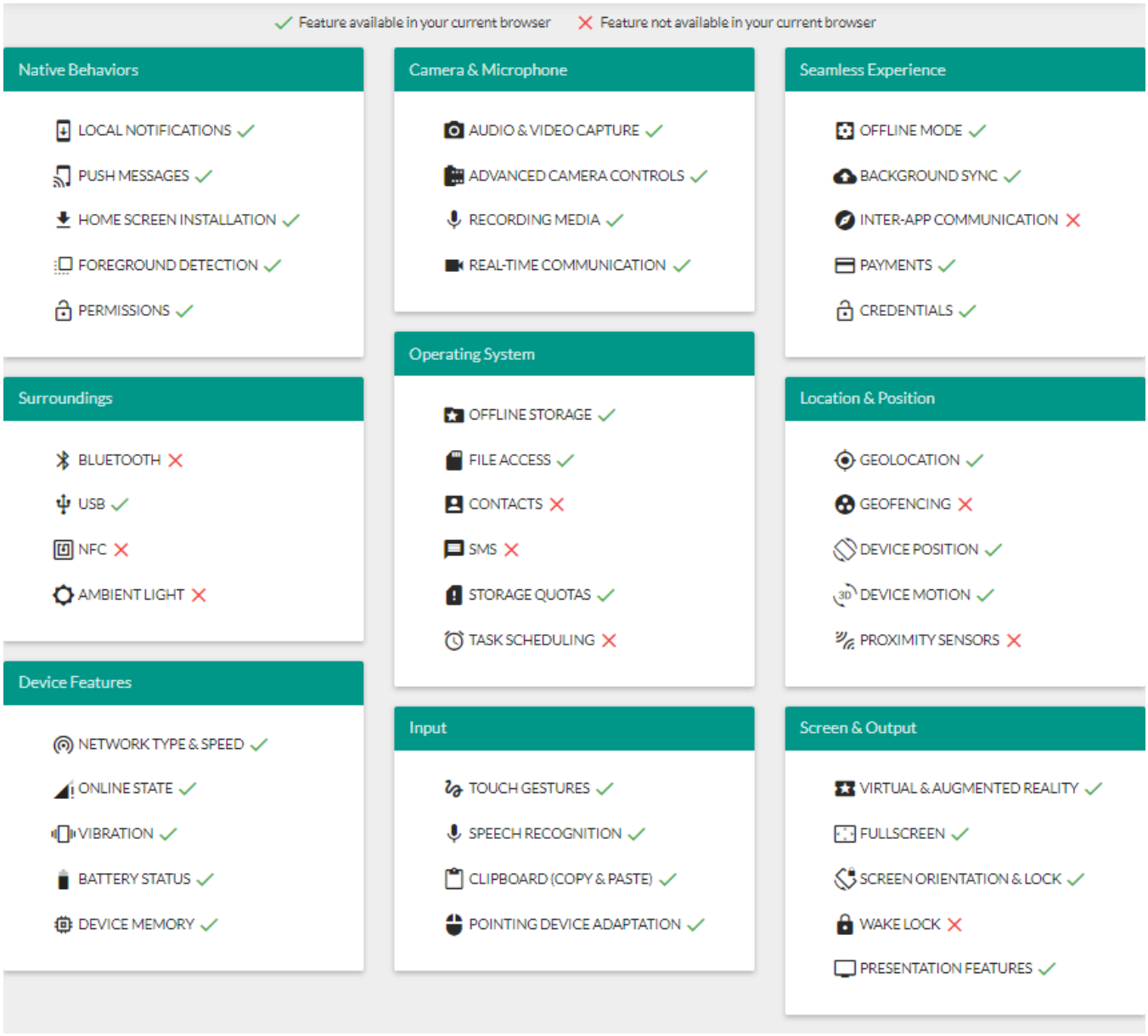

Fig. 3. A chart showing the functionality of Progressive Web Apps.

They offer the performance of a native app, while being platform independent (meaning they can run on most devices and core features are available in nearly every browser). Should we ever decide to integrate our mobile app with a website, making a PWA should mean there won't be much additional work. Lastly, developing a PWA instead of a native app will reduce friction in the data collection process because people won't have to be redirected to the app store and wait for an app to download.

C. Xamarin

Xamarin is an app development platform created by Microsoft that allows a single codebase to be deployed to Android, iOS, and Windows operating systems. In this regard, it is similar to a progressive web app. But unlike Progressive Web Apps, Xamarin offers no native browser support. A comparison from someone who has worked with both Xamarin and Progressive Web Apps came to the conclusion that PWAs are probably the better choice for simple apps (which is exactly what we want to make).[5] For the reasons listed above, our preliminary choice is to make a PWA.

V. Collecting Sample Data

We have already begun collection of sample data from friends and acquaintances. So far we have two sets of instructions. We have taken several pictures for each instruction set for the purpose of comparing the efficacy of the instructions. Pictures are expensive, so the fewer bad pictures participants in the survey make when taking pictures, the less money we have to spend on data collection and the better our app will be.

VI. Advertising and Reengagement Campaigns

In order to collect the labeled images we need to train our neural network, Karate Health will advertise on platforms such as Facebook with ads targeted at people with rheumatoid arthritis. This is their area of expertise, and the juicy details are somewhat of a trade secret of which none of us have knowledge. So a discussion of specific techniques is beyond the scope of this review.

After the initial round of advertising, we will target people who submitted pictures with reengagement campaigns, which is basically showing more ads to people who clicked on the ads last time. The motiviation for this strategy is the simple assumption that people who clicked on the ad last time are more likely to click on it again than the average person.

VII. Survey

In addition to taking pictures of patient's hands, we will be providing them with a short survey containing questions about their disease. Most of these questions will be picked by Karate Health. The results of this survey will help them hedge their exposure in case the neural network we create with the labeled images turns out to have no commercial value. If so, they will still have the results of the survey, which will have value by itself.

We will also include one or two questions of our own on the survey that will be used to label the images for use in training the neural network. Deciding which questions to ask is a crucial consideration for our project. Neural networks asymptotically approach the accuracy of the labels of the images with which they are trained. So the accuracy of our network will be limited by the accuracy of our labels. Our preliminary plan is to use swollen joint count or tender joint count as our label because that is easy for people with the condition to measure.

[1]University of Manchester, 'Study reveals enormous advances for rheumatoid arthritis patients', 2017. [Online]. Available: https://medicalxpress.com/news/2017-04-reveals-enormous-advances-rheumatoid-arthritis.html. [Accessed: 11- Nov- 2018].

[2] No author given. 'Arthritis Treatment: Early is Best', No year of publication. [Online]. Available: https://www.arthritis.org/about-arthritis/understanding-arthritis/early-arthritis-treatment.php

[3] T. Pincus, T. Sokka, 'Quantitative measures for assessing rheumatoid arthritis in clinical trians and clinical care', 2003. [Online] Available: https://www.sciencedirect.com/science/article/pii/S1521694203000779

[4] GO Corporation - Introducing PenPoint (1991). City unknown: GO Corporation, 1991. Available: https://www.youtube.com/watch?v=

[5] https://xamarinhelp.com/pwas-vs-xamarin-forms/