Application of Mobile Games to Support Clinical Data Collection for Patients with Niemann-Pick Disease

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Abstract - Collection of clinical information can be a fraught and intimidating process in hospital environments, especially for children with neurological conditions. Gaming and mobile technology offer many potential advantages for data collection where clinically important data can be collected as a side effect of playing games. Niemann-Pick Disease (NPD) is one example of a condition where gaming technology has the potential to greatly help patients and doctors alike. NPD is a severe, often fatal neurological condition where extensive physiological and cognitive information needs to be collected by doctors, typically in hospital environments. To help healthcare providers collect far richer information on NPD patients and reduce the burden/stress of patients and their families alike, a suite of targeted mobile games was developed to capture specific clinical information on NPD patients. These were evaluated with NPD patients and the feedback received was used to tailor the games accordingly. Personalised clinical information obtained through game playing was recorded, analysed and visualised through a flexible and extensible Cloud-based solution including capabilities for tracking patients longitudinally. This work has been directly aligned with the International Niemann-Pick Disease Registry. We suggest that this approach offers the potential for improved processes for data collection and importantly, a less stressful and more cost effective approach for collecting clinical information from and for patients. (Abstract)

Keywords: Mobile games, Niemann-Pick Disease, data collection.

I. INTRODUCTION
Mobile technology is increasingly pervasive and has many advantages for data collection, especially in a clinical/biomedical context. This paper focuses on the development and application of mobile gaming technology in the context of a rare but severe condition: Niemann-Pick Disease (NPD). NPD is a set of inherited metabolic disorders that are gradually debilitating and often lead to premature death [1,2]. There are three main types of NPD: Type A, B and C. Type A is most prevalent but has an extremely poor prognosis, with most cases being fatal by the age of 18 months [3]. Type B (adult onset) and type C have a better prognosis, with many patients with these disorders living into their teens or adulthood [4]. Often adult patients suffer from one or more cognitive disorders such as minor depression/bipolar disorders through to schizophrenia.

There is no cure for NPD at present however a range of treatments are available that can help patients manage their conditions. The International Niemann-Pick Disease Registry (INPDR – www.inpdr.org) is an international collaboration between scientists, clinicians and patient associations focused on better understanding and management of NPD. The INPDR aims to share information by collating anonymised patient data from across the world in a consistent format. In so doing it aims to gain knowledge and insight through establishing the natural history of NPD (types A, B and C).

The INPDR collects an extensive range of clinical/physiological information related to the progression of the disorder in NPD patients. The hypothesis underlying this paper is that mobile games can be used to collect targeted information on NPD patients in a manner that is scientifically sound; supports continuous real-time data capture, and essentially offers a new user-friendly model for patient data collection outside of a potentially inhibiting hospital environment.

The mobile games that have been developed have been explicitly designed to capture a range of physiological and cognitive characteristics associated with NPD patients. For many patients, external symptoms can include distended stomachs (due to enlargement of their spleen and liver); they can find it hard to coordinate their arms, hands and body more generally with minor aperiodic tremors to uncontrollable limb movement and seizures; they sometimes find it difficult to swallow and/or speak; they can find it difficult to remember, control their eye movements; identify certain colours and suffer from a range of other cognitive functions. Each of these can have ranges of severity: from minor imbalances (occasional falls) and moderately slurred speech through to being fully bed-ridden and unable to speak.

For diagnosis and on-going treatment, clinical/medical testing is commonly used where patients are required to undergo a range of clinical tests, typically in hospital settings. This can include blood tests, MRI/PET scans, DNA/genetic testing, through to a range of physical and cognitive tests that measure aspects of the condition. Whilst many tests implicitly require patients to attend clinics, e.g. for extraction of blood or scans, many more tests can be done without the physical attendance of patients in a clinical setting. For diseases such as NPD, the scarcity of patients usually imposes a significant burden on particular healthcare institutions and/or the affected families since clinical experts (typically neurological experts) are not always available. Given this, access to experts can require patients and their families travel extended distances to see experts that can help and support them with their condition. Periodic checks (typically every 3-6 months) means that asynchronous patterns of patient management occur.

The INPDR went live in September 2014 and currently (March 2015) includes (Figure 1) 62 NPD patients from across Europe (57 NPC and 5 NPAB). Each patient has extensive phenotypic and genotype information that is included in the registry including their background demographic information; laboratory diagnosis; family history; clinical history; treatments they are receiving; clinical trials/studies they may be involved in, and most importantly here - their associated disability scale (Figure 2). The data is longitudinal in nature, i.e. patients are seen repeatedly and the progression of the disease and response to treatments are captured.
The disability scale includes detailed information on a range of aspects of their disability: their ambulation (from normal – wheelchair-bound); their manipulation (from normal – severe dystymia/dystonia requiring assistance in all activities); their speech (from normal – absence of communication); their swallowing (from normal – nasogastric/gastric button feeding); eye movements (from normal – complete ophthalmoplegia) and seizure information (from no seizures – seizures resistant to anti-epileptic drugs). These scales are used to calculate an overall level of disability as shown in Figure 2.

These data sets are captured in a clinical context. The premise of this paper is to explore and show how (mobile) gaming technologies can be used to automatically capture these disability scale components focusing specifically on manipulation and eye movements. Work is ongoing to extend the portfolio of games to cover other aspects of their disability, e.g. ambulation and mobility. This data should be collected in a user-friendly manner and allow patients to undertake a more direct role in managing their condition, providing regular updates to doctors tasked with monitoring their condition. Visits to specialist hospitals can be avoided if the doctor can see that the condition is unchanged through seeing the results of games directly for example.

The possibility for remote diagnosis and management has typically been the field of telemedicine, however games for health offers a new paradigm data collection. This frees up more time for the physicians and nurses to provide advanced care when they eventually do meet the patients. In this way, games for health delivered through mobile devices has the potential to provide efficiency and financial benefits for hospitals and patients alike, and ultimately change the paradigm of coordination with doctor-patient relationships.

II. RELATED WORK

Several others have previously explored gaming technology in a healthcare context. Under the support of Games for Health project [5], a range of cutting-edge games and gaming technologies were developed to improve health and health care. More recently with advanced graphics, improved realism and attractive interactivity, computer and video games have been used to solve a number of health and health care issues, especially in relation to chronic disease treatment, physical rehabilitation, weight management and potential disease outbreak prevent [6,7]. Compared to traditional approaches, game-based solutions motivate and engage users in a way that no other medium can.

There is no doubt that technology is changing the doctor-patient relationship in many aspects: records management, symptom assessment and preventive and corrective procedures [8,9]. However the utilization of games for health offers new dimensions to the patient care model. Patients are not only the objects being treated and monitored but also they can/should be involved in the process of their own health care management. Other areas that health care games have been used include: weight and nutrition management; cognitive behavior and mental health; disease prevention, self-management and adherence; clinical training, simulation, diagnosis and treatment; rehabilitation and therapy, and home-to-clinic telehealth systems [10].

Pervasive and ubiquitous mobile technology has shown that it can encourage people to pay attention to their life and health more generally [11,12]. Currently, the majority of health games are exer-games, which encourage players to do exercise or various forms of physical activity. For example, the fitness games developed by Mueller et al [13] allows people to complete physical activity sessions by simulating varieties of sports (like playing a ball game and running) with remote third parties. The Chinese Aged Diabetic Assistant provides a game in which patients are required to choose a traditional Chinese mask that matches their mood [14]. The application successfully empowers patients to understand diabetes, track their health condition and follow a healthier lifestyle. Shadow Boxer [15] allows players have to physically move their arms to punch a virtual target. A wide range of electronic games have been developed offering a range of contributions in promoting wellness by teaching players about healthy living. The Nintendo Wii is one platform explicitly designed with a range of gaming / health opportunities. Recent versions of the iPhone itself include a health-monitoring app as part of the basic operating system. This automatically calculates the number of steps taken and a range of other physiological information (e.g. heart rate) with self-recording features such as nutrition monitoring.

The emergence of mobile devices offers a highly evolved platform on which to develop, deliver and play games. With the fast development of smartphone and tablet technologies, games are increasingly being delivered to mobile devices that leverage advances in technologies, e.g. built in accelerometers. However despite the above list of examples, targeted games for complex clinical conditions are less ubiquitous. With the improved performance of mobile devices now available with touch screen and sensors and the ubiquity of mobile devices across society more generally, the development of games for complex clinical conditions has many potential benefits especially compared
with traditional devices, such as computers and televisions. Mobile devices have four main advantages:

- **Portability**: compared with traditional computational or content delivery devices, mobile devices can be taken everywhere. Moreover they are lighter and more portable, so players can play the game anywhere and at any time.
- **Accessibility**: with the popularity of the Internet and high-speed wireless networks, mobile devices can communicate with servers and other devices whenever and wherever they need.
- **Operability**: mobile devices have better operability than traditional devices. Almost all mobile devices provide touch screens, which makes their operation simpler and more convenient than traditional devices, which often required physical input devices such as a keyboard and a mouse.
- **Functionality**: mobile devices may not yet be as versatile as laptops in terms of functionality, however for entertainment, mobile devices often provide better dimensions of performance than laptops. For instance, the integrated sensors offer functions such as recognizing orientation and measurement of angular rotation, location, movement and speed.

Based on these advantages and the fast improvement in hardware components of mobile devices, games for health in mobile devices are rapidly becoming a new domain attracting considerable attention.

III. SELECTION AND DESIGN OF MOBILE GAMES

There are several dominant mobile operating systems: Android, Apple iOS and Windows phones. They all have their own advantages and disadvantages: popularity; affordability; simplicity; application (app) stores; availability of Cloud storage and security. In this work it was decided to develop the initial portfolio of NPD games on the Android platform, however work is currently ongoing to develop an iOS version of these games. Android is itself based on the Linux kernel and has been developed by Google. It is under open source license and designed primarily for touchscreen mobile devices – a key requirement for the gaming interface and recording of patient disability information.

Based on the requirements of the project, the system architecture is divided to two parts: the Android app side and the resultant visualization/analysis side. A Client-Server architecture was adopted in the development of the Android app with a browser-server architecture used to analyze and present the game results. The main Client-side activity is to launch and control the app and the games. The client plays a scheduler role in the whole application and is able to control which view should be displayed. Initially, the app starts with a welcome view (Figure 3 (left)) and then redirects users to a login activity. If the user logs in successfully (using their unique identifier from the INPDR as a username), a menu view is shown (Figure 3 (right)) that lets them choose the game they wish to access/play.

In designing the NPD games, numerous meetings and discussions took place with the NPD domain experts – this included neurologists from the Royal Melbourne Hospital. Based on these discussions and the demands and challenges facing NPD patients, the games were designed to cover specific handicaps of NPD patients, namely: hand control, eye movement, cognition, memory and mental agility. Six games were designed to assess levels of (potential) patient disability as shown in Figure 4. We summarise the idea behind each game and the disabilities they were used to measure.

A. **Pipe Game**

The basic premise behind this game was to measure hand/eye coordination – a key challenge for NPD patients [4]. Players were expected to move their finger along the tunnel and not touch the sides. Each level has progressively more difficult tunnels (narrower and with more turns). A timer in each level is used to record the time the player takes to pass the level. Irrespective of whether the player passes or fails the level, all details are recorded. If the player completes the level, the level and the time taken are used to establish the score that is stored in the patient database. If the player fails the current level, the score, the time, the percentage of the game finished, and the statistics on the current game level are stored in database for
review by the patients and/or their doctor. This game allows doctors to judge the patient’s level of controlling their muscles and hands such as horizontal movement problem and vertical movement. It is noted that with NPD patients, horizontal movements tend to be more challenging for patients.

B. Drift Ball Game
The Drift Ball game was developed to keep track of NPD patients’ ability to control their muscles and especially their balance. The premise of the game is for the patient to keep a ball (red circle) within a given area (the grey circle) (Figure 4). The ball itself gradually (randomly) moves and corrective (balancing) actions must be taken. This requires that the player makes judgment on the ball speed and direction, and then reduce the ball speed to zero or less before it collides with the area boundaries by tilting the device. By tilting the device, the drift of the ball should be corrected to keep the ball on the plate. Muscle and balance control can vary between ages for NPD patients. For those older than 15, dystonia is one of the most significant symptoms [1]. This game uses the in-built accelerometer to monitor a patient’s ability to keep the device steady and if so, for how long. Different levels of difficulty can be set with smaller circles to keep the ball within, increasing ball velocity and increasing sensitivity to movement. A game level is completed if the patient keeps the ball in the circle for 20 seconds.

C. Card Memory Game
Nearly a third of adult NPD patients have dementia as the prominent form of cognitive disturbance [4]. To help doctors monitor their patients’ cognitive competence and/or memory, the traditional card memory game was enhanced. As with traditional memory games, a target card and some optional cards (including one matching card) are given at the beginning of each round. These are displayed for a few seconds before being turned over (hidden). The player needs to pick out the card that matches the original target card. The game has gradual levels of difficulty with increasing numbers of optional cards and decreasing amounts of time to see/memorise the optional cards before they are hidden.

D. Balloon Game
The balloon game is a simple but classic game. The basic premise of the game is to pop balloons of a certain colour moving up the screen before they reach the top. For the average person, this game is trivial. However for NPD patients, this game can be quite challenging and tests a range of abilities. Firstly the player needs the ability to distinguish different colours (often non-trivial for NPD patients). Secondly, the players should have the ability to control their fingers to point at the accurate position of the balloons and pop them. Thirdly, the reaction needs to be quick enough to pop balloons before they disappear. When the screen is large enough, the game can also assess the ability of NPD patients to control their eye movement, since vertical gaze palsy (the inability to move the eyes up and down) is another characteristic of NPD. The players are required to avoid balloons in given colours, e.g. don’t pop yellow balloons, but pop all others. To measure reaction and hand control, the speed and the number of balloons increases with each level. The time limits are from when the balloon runs into the screen to the time it disappears. If the player cannot pop the balloon before it runs out of the screen, the game is over. Alternatively if the player pops an incorrect balloon, the game ends.

E. Breakout Game
The Breakout game is a traditional game that can measure a range of NPD patient abilities: vertical gaze, horizontal eye movement paralysis and whole eye/body co-ordination. This version of the Breakout game is similar to traditional versions except that players need to scroll on the tablets’ screen to control their paddles. In order to make this game suitable for NPD patients, a few elements of the game were modified. Firstly, the number of targets was modified to increase the chances of success. Secondly, due to the physical challenges facing these patients, the ball speed was reduced compared to traditional versions of Breakout. Thirdly, only two levels were set in this game to make those patients feel more confident – recognizing that continuous failure can be detrimental to patients who should be positively encouraged to play the games. Fourthly, unlike traditional versions of Breakout that increase the ball speed as the game progresses and more levels get completed, this version does not. Instead the width of the paddle is reduced. The patient’s current score and their highest score are displayed on the screen to give a hint on how many points they need to surpass their own record. Other related information like the current game level is also displayed.

F. Choose Colour Game
NPD patients have a range of cognitive challenges – this includes colour identification. As such it is important to design a game that can test the ability of patients with regard to colour recognition and cognitive abilities more generally. Considering this requirement, the Choose Colour Game was created. The main aspects of this game are capturing information on whether the patient can distinguish different colours, and importantly how fast their brains can switch between different input signals. The game contains two elements: the colour (ink) and the word itself. The colour of the ink is different from the word’s meaning. The sentence in the middle of the screen is used to decide which block at the bottom contains the right answer. It randomly switches between “Choose the colour of the Ink” and “Choose the meaning of the Word”. The player must choose the appropriate block before the time limit. In the example shown in Figure 4, the grey block (bottom right) must be selected, and not the colour red in which the word (Grey) is written.

IV. RESULT ANALYSIS AND VISUALISATION
In order to explore game results, a website was designed as the front end to the central server used for data hosting, analysis and visualisation. This server was hosted on the National eResearch Collaboration Tools and Resources (NeCTAR – www.nectar.org.au) Research Cloud. The data itself was captured and analysed in a noSQL database (CouchDB).

In the first instance patients have to register on the centralised website using a targeted username/password. This
username is used to record their information in the database. The INPDR system has a unique identification, e.g. NPC-UKBI-27 is the 27th NPC patient from Birmingham, UK. It is emphasised that no patient identifying information is entered into the NPD registry or collected in the central (game) server. It is also the case that patients (and/or their families) may choose not to log in to such systems and are happy to leave the analysis and interpretation of the data to the doctors/medical staff.

For each game, there are several possible analysis and graphical visualization realisations. For example, there are three charts to present the results of the pipe game. In Figure 5, the red bar shows the highest score of the patient – in this case (dummy user) “test”, while the blue bar shows the highest score attained by all users in each level. Finer-grained specialisations are also possible, e.g. patients with given degrees of physical and/or cognitive handicap due to NPD.

In order to present the trends of the patient, game results for each patient can be sorted by time. Figure 6 illustrates results over different time periods for a given (representative “test”) patient.

The scores given are calculated based on a combination of the complexity of the level of the game, e.g. more complex pipe layouts and the time taken to complete the level (or the time taken to obtain the given distance achieved). This information allows doctors to observe the trends over time for a given patient. This information can be used as a key source of information for better understanding the medications and treatments that the user is receiving. Thus it is not the individual spikes in the data that are necessarily important but the statistical averages that indicate progressive improvement or regression in the physical and/or cognitive characteristics of a given patient.

For some games, such as the pipe game, an extra chart is provided that allows assessing the degree of completion of a given level of a game. This is shown in Figure 7 (for a dummy user). Such information can also be used to explicitly highlight the places where failures repeatedly happen. Thus horizontal movements can be challenging for NPD patients and this would show in the locations where the tunnel sides are touched (and games are ended), or alternatively where prolonged time periods are required to complete sections of the tunnel.

In order to assess the suitability of the games for NPD patients, NPD patients from Royal Melbourne Hospital were invited to play/evaluate the games (under the supervision of their doctor/consultant). Each patient had varying degrees of NPD – from obvious physical control challenges to less obvious challenges and slightly slurred speech.

Under semi-supervised guidance and a very brief tutorial, the patients played all of these games. These results were captured in the central server and subsequently analyzed. Initially it was assumed that the games would be too simple and would not allow for deeper levels of assessment by NPD patients. However this was not the case. Seemingly trivial games (such as level 1 of the Pipe Game shown at the top of Figure 7) had challenges for some of the patients. This feedback was used to refine the games and where necessary, reduce the challenges that they posed, e.g. increasing the width of the pipes. Similar game refinements based on direct experiences included reducing the speed and diversity of colours of the balloons. To cover the differences in the ability of patients, optional levels were also set in games. For example, games were extended to allow for patients to start from the place that they failed to complete the game.

A. Evaluation

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Feedback on the data collected was also discussed – including reassurance that the collected data was indeed non-identifying. The NPD patients (and their families) that evaluated the games were keen to see their own gaming profile and how they benchmarked compared to others. Further work will be undertaken to define suitable assessment and comparison criteria, e.g. to assess those patients with similar (minor - advanced) stages of NPD in much the same manner as that undertaken for competitors in the Paralympic games.

A key benefit of the games by the patients was recognition that their condition resulted in physical and cognitive impacts that were shared by others. Thus knowing that they were not the only ones unable to completed particular games or pass certain levels of games was important for them. The patient and families feelings regarding the functionality and difficulty of the games were captured. All were fully supportive of the work. It is hoped/expected that these applications will become de facto tools used to help capture information from NPD patients in the future. This will help improve doctors’ diagnosis as well as patients managing their own health.

V. CONCLUSIONS AND FUTURE WORK

Previous work on using gaming technology for healthcare have shown the great potential that games can provide to advance medical treatment for different kinds of patients. Well-designed games can enable doctors to monitor their patients’ performance remotely and more efficiently than before as the number of face-to-face medical tests can be decreased significantly. Games can also reduce patients’ mental burden and provide a new (fun) paradigm for clinical data collection. This encourages game play and provides a far richer resource than the snapshot (every six months) of data that is typically collected in clinical/hospital contexts. It is expected that this will reduce the burden of medical resources due to the decreased number of medical tests required, and face-to-face time with clinical consultants/doctors.

We have shown that the development of gaming and mobile technologies can be used to collect a wide range of clinical and physiological information designed with the specific disorder in mind. This work has focused explicitly on capturing physiological and cognitive information directly related to Niemann-Pick, however this is one example of a large family of neurological disorders. In the future, we see the opportunity to collect much more data across many more diseases through targeted mobile application development.

Many games can generate significant volumes of data that has increased computational demands (both for processing, analyzing and storing). We have used Cloud computing resources that allow the platform to scale with increased numbers of patients. Furthermore, to cater for the demands of data-intensive applications we have adopted the noSQL document oriented database: CouchDB at the back end of the analysis. This approach allows both the server and browser side of the application to scale through the cloud.

However, even though gaming and mobile technologies can make considerable contributions to improve the current healthcare situation, games or applications in themselves must be used with caution. Traditional medical tests are always likely to be mandatory for doctors to diagnose patients and monitor their conditions. Games and the data they can generate can be used to augment clinical information however they are not intended to replace existing data captured in a clinical context entirely. Nevertheless, we have shown that such technologies can indeed provide a novel platform that can greatly augment clinical understanding, through a form that encourages data collection by affected individuals. This has the potential to bring huge benefits to society in the near future.

The next phase of this work is to port these games to other mobile platforms (iOS) and ultimately conduct clinical trials related to the efficacy and suitability of the application. This will include improving the specificity and sensitivity of the games in capturing physiological and cognitive information.

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