Abstract

Mild traumatic brain injury (mTBI), otherwise referred to as concussion, affects 1.4 to 3.8 million Americans per year (Faul, 2010). Despite a crowded screening market for mTBI, there are no reliable, accessible tools for on-site screening. Therefore, it often goes undiagnosed and untreated which ultimately can lead to significant economic and health problems. The purpose of our product is to serve as an on-site objective, accurate screening tool for mTBI. The TBeye Tool will achieve this by building on existing smartphone technology with an add-on device to aid in data collection and an application to use the phone's processing abilities to implement an innovative analysis system for mTBI screening. Our design was developed under FDA design regulations and followed the Stanford Biodesign Process. The prototype has shown promising results, reliably differentiating a healthy subject from an unhealthy one ($p<.05$). Due to its low cost and ease of use, our solution has potential to permeate numerous markets on a global scale.

The Problem

Significance of an Early Diagnosis There are about 1.4 million documented cases of traumatic brain injury in the United States per year (Cecil et al., 2011a), with about 85% of those estimated to be mild (Buck, 2011). There is growing concern over the number of cases being undiagnosed because the symptoms are subtle, take a while to set in, and largely rely on a patient's ability to openly recognize the severity of their own symptoms. Additionally, both sports and military patients are resistant to reporting their injuries. This is partially because healing time presents a barrier to their goals and also due to a misconception that suffering from mTBI is like suffering from another physical injury that can and should simply be powered through (Buck, 2011; Haley, 2014). There are no broad estimates for how prevalent actual mTBI occurrence is. However, a few studies have shed enough light to indicate that underreporting is a significant issue. For instance, over half of American high school football players admitted that they did not report concussive symptoms to their coach (Buck, 2011). Surveys of NFL players indicate a similar find – 56% claimed they would hide a concussion to keep playing ("NFL concussion poll: 56 percent of players would hide symptoms to stay on field," 2012). Even more extreme, only one in 30 concussions were found to be reported in one Canadian youth hockey league (Buck, 2011).

Mild traumatic brain injury has just within the past 15 years or so been recognized as a serious problem that needs to be treated. In the first few days following mild brain injury occurrence- and not necessarily immediately – symptoms ranging from nausea to vision problems, aggressiveness, and cognitive deficiencies may show up. If the injured person goes undiagnosed and therefore untreated, symptoms can persist for years. After a year, 44-50% of mTBI patients still show persistence of three or more symptoms (Kan, Ling, & Lu, 2012). mTBI occurrence leads to an increased risk of developing depression, cognitive deficiencies, and neurodegenerative diseases over the long term (Buck, 2011; Kan et al., 2012). Individuals with a history of TBI make up an unproportional amount of individuals that are homeless, unemployed, or in prison (Buck, 2011).

The estimates on how much money treating and diagnosing mTBI saves easily reach billions. The cost of treating an individual for a short time is much more cost-efficient than the lost money over the long term due to decreased productivity, issues due to increased risky behavior, and other slowly-developing side effects. One "conservative estimate" claims that over 50 years, improper care of TBI patients will result in $288.7 billion lost tax revenues – when immediate treatment costs the government just 1.7% of that figure ("Factsheet - COSTS of Untreated Brain Injuries Caused by Traumatic Brain Injury (TBI)," 2011).

Treatment of mTBI is often as simple as taking a short break from normal activities followed by a gradual reintroduction to everyday practices, yet premature return to activities is a frequent problem as many mTBIs fail to be identified at all (Master, Balcer, & Collins, 2014). Aggravating recent brain injuries has severe and potentially permanent implications on psychological and neurocognitive health, which could be prevented if a reliable in-field assessment was available.

The Market The first step to getting treatment for mTBI is getting screened properly, yet there are gaping deficiencies in current screening tools. The most popular tool for patients in which taking a baseline is feasible (such as sports or military groups) is the ImPACT (Immediate Post-Concussion Assessment and Cognitive Testing) program. This is a computer based neurocognitive test that can conveniently be accessed on a smart device. However, it is notoriously unreliable – studies of healthy patients found that 28 to 46 percent of participants show false positives for concussion occurrence (Broglio, Ferrara, Macciocchi, Baumgartner, & Elliott, 2007; Resch et al., 2013). Additionally, the results require training to interpret, and patients can fool the test. Other commonly used neurocognitive tests include the King-Devick Eye Movement Test, which does provide objective output but requires baselines that can be falsified. Combination neurological/physical tests that do not require baselines include the SCAT (Standardized Concussion Assessment Tool) series, which relies both on a patient's own and often inaccurate assessment of their state of mind and subjective observations on part of the physician. Its conclusions take into account factors based around the Glasgow Coma Scale, developed for moderate to severe head trauma but not at all appropriate for assessing mild trauma. The MACE (military acute concussion assessment) is very similar to the SCAT series. According to Sgt. Major "Archibald", a military medic whom we sought out while researching the military market, claimed there are problems with the test including: it is easily sabotaged by soldiers memorizing answers, it can only be administered a limited number of times before losing utility, it is not sensitive enough, and symptoms often go underreported due to the macho culture (Price, 2013). Most importantly, he did not trust the test results that are based on subjective evidence – a subjective report of symptoms followed by a subjective conclusion. More thorough assessments are available, but not performed due to their excessive administration time (Miller & Zwerdling, 2010). Finally, none of these tests are suited for patients that do not have baselines available. Sports and military are the most notable populations in which taking a baseline is feasible, yet represent respectively only about 330,000 of the estimated 1.7 million total annual TBI occurrences in the United States (Defense and Veterans Brain Injury Center, 2013; University of Pittsburgh, n.d.). The majority of concussion patients are more likely to be treated by an EMS or taken to the emergency room, where no concussion tools are marketed and assessment consists exclusively of subjective observations and conclusions, a loosely interpreted variation of the ImPACT program. Finally, the high cost associated with these tests restricts its accessibility for poorly funded groups or individuals.

Our Goal Based on our research into the problem and our interviews with a military medic, a National Football League Doctor, a sports medic that specializes in concussion research, high school sports coaches, athletes with histories of TBI, and EMS personnel we identified the need to address:

Head trauma patients need accessible, objective, and accurate on-site screening for mTBI.

Our initial need assessment focused on the military, but as our design progressed we expanded our scope to professional and amateur sports and emergency settings. These markets share similar enough needs –device resilience, timely assessment abilities, low cost, low training hurdles, etc. – that our solution has potential to permeate into other sectors with minor modifications.

The Design

Overview of the system The TBeye Tool is our solution to this need. It is a mobile rapid-assessment application that utilizes the video and processing capabilities of an existing smart device to obtain pupil reaction information and processes the data collected to output numerically the likelihood that mTBI has occurred. We have also created an eyepiece attachment to maximize accuracy. This add-on may be optional in later versions of the TBeye Tool, but testing to ensure that sufficient reliability is maintained even in the presence of ambient light must be done first.

In its current phase, The TBeye Tool has two major components: a hardware part in the form of an eyepiece that produces specific light while blocking out external ambient light, and a software part in the form of a smartphone application. The eyepiece is attached to the phone by a simple clip design that will fit the majority of smart phones and tablets. The eyepiece consists of a durable plastic that is resilient against force impact and extreme environments, along with a soft rubber piece similar to that found on binoculars. It houses 2 red and 2 white LED lightbulbs, a button battery, and will communicate with the phone either by USB or wirelessly. Figure 1 shows a simplification of the TBeye Tool in action.

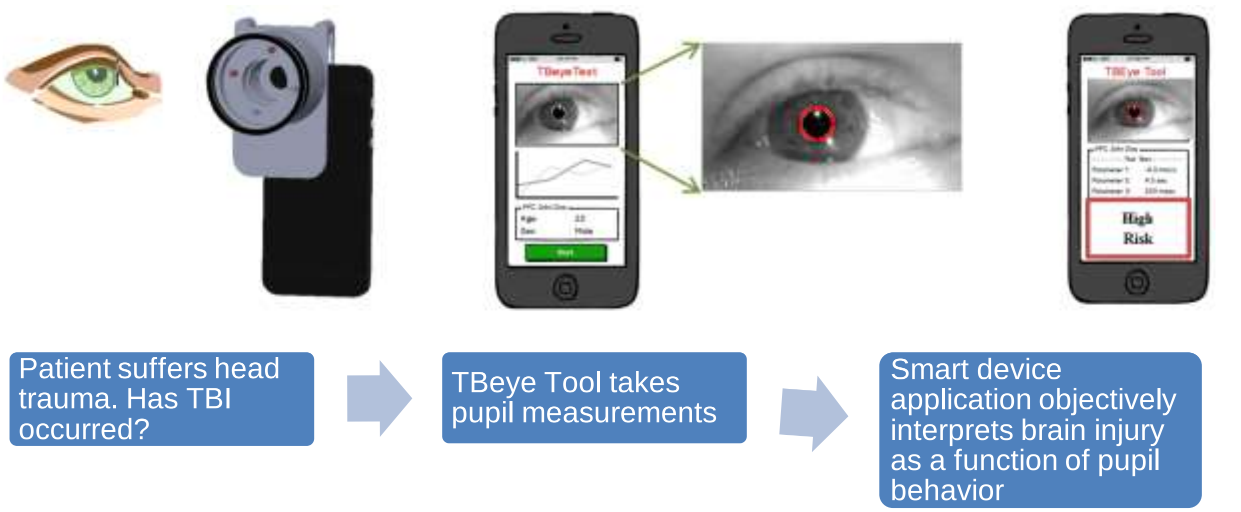


Figure 1 The TBeye Tool for concussion screening - simplified

From the user perspective, operation is simple and requires little to no training for anyone already familiar with smart devices. Setup takes less than a minute and consists of simply opening the application and clipping the hardware on to the phone or tablet. Once the application is opened, the application instructs the user with step-by-step instructions. First, the user is given the option to either take measurements relative to a specific patient or to take measurements anonymously. There are a few important differences between these options because of the way our data is processed. In populations that have a high likelihood of concussion such as sports teams or military groups, it is recommended that each patient take a baseline test at some point prior to concussion. The ocular measurements taken in the post-concussion test will then be compared to the specific patient's baseline data. Since there is some variability in eye behavior between patients, this option would provide the highest accuracy in determining how likely a concussion has occurred. If the patient has no baseline data stored in the phone, they may compare their measurements to those of an age-paired, generalized healthy population instead.

Once the user has determined whether a patient has baseline data stored or not, a screen similar to that seen in figure 2 follows. To take an ocular measurement the user holds the TBeye Tool up to the patient's left eye and asserts enough gentle pressure to assure firm contact and block out ambient light. If the eyepiece is not used, the phone should be held about 3 inches from the eye and ambient light minimized. When ready, the user taps "start" and the TBeye Tool or the mobile device's flash will first shine the white lights in to the patient's eye to cause pupil contraction. If the add-on is used, the red lights will then shine – this will allow the pupil to dilate while still providing enough light for the camera to obtain video footage of the pupil's reaction. Without the hardware add-on, video of the pupil's reaction will still be taken at some cost of precision. The user will repeat this data collection process on the other eye. The application will then process the data taken and compare it to the baseline or comparison data available before outputting a percentage value indicative of the likelihood that TBI has occurred. The test takes less than two minutes to administer and process, and the baseline just less than three.

Looking to the eyes as an indicator of concussions is not a foreign concept – the swinging flashlight test is part of the normal assessment. When head trauma occurs, the integrity of the third cranial nerve which controls the pupil is challenged by shearing forces. Secondary swelling of the brain also occurs after injury, leading to increased intracranial pressure that compresses the nerve and further inhibits its function. Changes in pupil reactivity due to head trauma have been well documented (Capo-Aponte, Urosevich, Walsh, Temme, & Tarbett, 2013; Cecil et al., 2011b; Taylor et al., 2003a, 2003b). The magnitude of significant pupil behavior variance from its normal behavior is on the order of .01 seconds, too small for observers to visibly gauge (Taylor et al., 2003a). The TBeye Tool provides a significant increase in the degree of sensitivity over the bare eye so that the small discrepancies between normal, healthy populations and brain injured patients may be detected.

We are currently taking three pupil response parameters into account which, to our knowledge, are not currently used by any other concussion assessment: constriction latency, 75% recovery time, and dilation velocity. These parameters have shown statistically significant differences between populations of healthy patients and post-mTBI injury age-paired patients at $p<.05$ (Capo-Aponte, Urosevich, Walsh, Temme, & Tarbett, 2013; Taylor et al., 2003). A fourth parameter, pupil asymmetry, is known to increase after injury, but patients will require a baseline in order for this parameter to be factored in – natural asymmetries of up to .5 mm are known to be present in an uninjured population, and up to 20% of the population show up to a 1 mm difference in natural pupil diameter (Capo-Aponte et al., 2013; Taylor et al., 2003b).

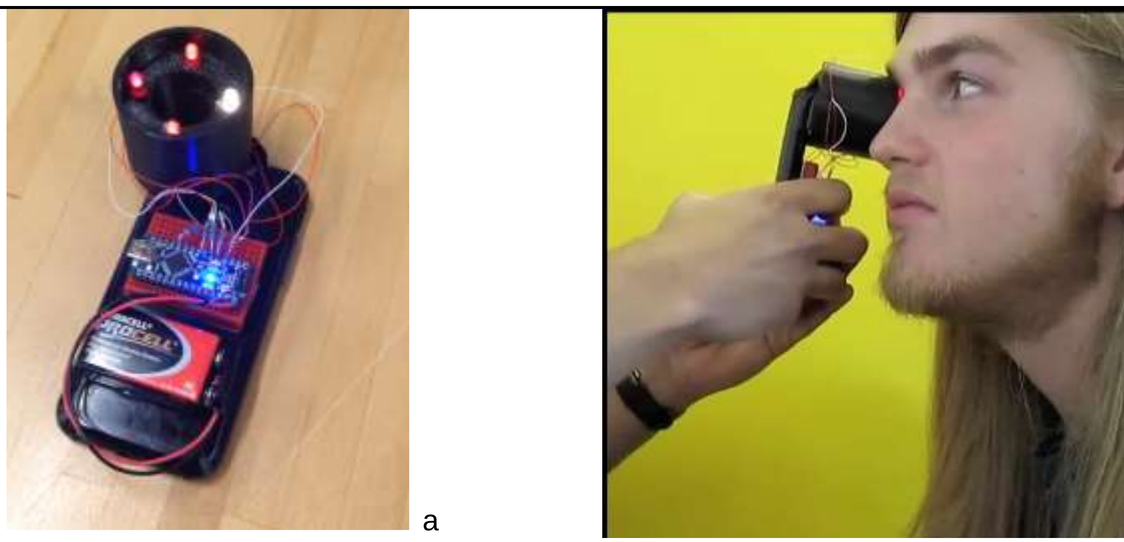
Innovation There are a few key innovative features that we have focused on developing. First most, our system of analysis and output is unique and not only directly addresses the market needs for a purely objective analysis of whether or not mTBI has occurred, but does so in a way that provides a higher level of accuracy than more commonly used tests. This advantage over other systems is because the input is exclusively objective, versus some other input methods that can be faked such as many neurocognitive tests. Additionally, the analysis of the results is also objective, versus tests that require a coach or medic to gauge subjectively the results of an analysis. Second, it conveniently integrates common phone features. This makes it affordable to manufacture, easy to implement, and ideal for data storage and transfer. These resulting characteristics give the TBeye test a huge market advantage. Expense was a major factor we considered in ensuring "accessibility". Other innovations include the device's durability and compactness. Many tests for concussions are limited to the hospital setting due to sensitivity or bulkiness. Use of red LEDs to increase imaging contrast is also an innovation. Most pupillometers use infrared light to enhance imaging contrast. However, IR is more expensive and has potential to be filtered out by some mobile cameras. Therefore, our economical red LED light for enhancing image contrast is a practical improvement.

These innovations have been filed under a provisional patent.

Final Product Potential The TBeye Tool offers a significantly more objective and accurate concussion screen than any other solution on market and at a significantly reduced cost. We have made significant efforts to ensure our product meets the needs of the market by regular consultations with our potential end users, ranging from concerned parents with athletic children to military medics. Ultimately, we hope to expand our efforts globally – third world countries have a higher rate of concussion than their developed counterparts, and more people are able to access phones than they can toilets (UN News Service, 2013). Hence, we plan on expanding our highly accessible solution to a much larger scale so that all individuals can have the knowledge and opportunity to protect their physchological and neurocognitive health. Additionally, our solution has potential to expand beyond concussion screens as a screen for neurodegenerative diseases and drug/alcohol usage as well.

Evidence of a Working Prototype

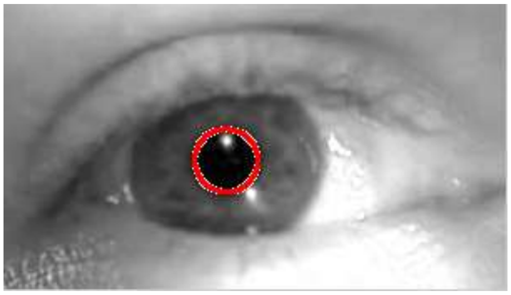
Hardware The prototype eye piece was 3D printed out of ABS plastic. An Arduino microcontroller is used to control the four LED lights, which automatically flash for a preset time. Video footage is obtained using the phone's video recording option. In later increments of our product, the phone will control the hardware. Figure 2 shows our prototype in use.



a b

Figure 2 Prototype Hardware

Software Video footage was fed into matlab for processing. For our prototype, we have developed a script that will automatically detect the patient's pupil and record its radius over time. This script will be part of the downloadable application in future installments of our solution. Figure 3 shows an example of data collected using our automatic pupil detection system.



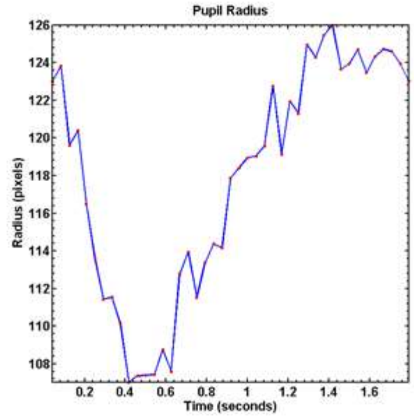


Figure 3 Patient's pupil dimensions are automatically detected and recorded against time

Using this data, we were able to obtain the patient's recovery time and constriction latency. For example from the data set charted in Figure 3, taken from a 22 year old male with no history of TBI, 75% recovery time and constriction latency were found to be 1.15 seconds and 200 milliseconds respectively.

Process Validation To test our program, eye footage was obtained from a healthy patient with no history of TBI. The output data was analyzed for two features: 1) the healthy patient data fell within the expected range for a generalized healthy patient and 2) the healthy patient had limited variation over time. Particularly in neurocognitive tests for concussions, baselines have been shown to be a problematic source of variability.

For this particular patient, a healthy 22 year old male with no history of TBI, average 75% recovery time was 1.458 ± .177 seconds (mean ± SD). Using the student's t-test in regards to 75% recovery time, we were able to successfully identify our patient with the healthy population at a significance of $p<.05$. These parameters assume that our 22-year old male is similar to the average soldier. Variation seen may be due to differences in age or gender between him and the healthy summary population statistics. A more specific comparison of what his parameters should be is not available, because there is no published baseline data for reference, partially due to the unavailability of tools such as the TBeye Tool that can obtain this data. Nevertheless, our patient data more closely resembles that expected of a healthy patient, indicating that we could reasonably conclude that even with no other knowledge available, this patient is more likely healthy that concussed. The consistency between days is also very positive, indicating that this baseline data is stable, reliable, and not easily confounded by unknown variables.

We are currently in the process of modifying our design so that it is suitable for clinical testing as per FDA Medical Device Standards. We have made connections with research physicians in neurocritical care that are willing to work with us in writing IRB-compliant study proposals and provide clinical resources necessary to obtain TBI patient data. We are also working on translating our program from a computer to a smart device application, working around device limitations such as camera resolution to ensure integrity of the system is kept intact.

This device will be available to populations with baseline data sooner than those that cannot obtain baseline data because a general population parameter database must be built up for those individuals. Factors that must be taken into account when creating our database include but are not limited to age, drugs (prescribed and otherwise), and neurodegenerative diseases.

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