1. **Research Proposal**

**Facial Recognition to Predict Acute Pain and opioid requirement after Surgery**

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**Aims of the Study**

*Primary Aims:*

1. To quantify the unconscious patient’s level of nociception (loosely, “pain activation”) before recovering from general anaesthesia immediately at the end of surgery, until they regain consciousness, using 3-D facial mapping technology.
2. To measure the correlation between patterns of facial mapping present (using 3-D facial mapping technology) after administration of intravenous opioid prior to commencement of surgery and duration of opioid requirement following surgery.

*Secondary Aims:*

1. To explore the micro-expressions of pain in unconscious patients as outlined in the facial action coding system (FACS).1,2
2. To characterise and automate the facial expressions component for the Behavioural Pain System (BPS).3,4
3. To correlate facial expressions occurring after receiving opioid therapy as part of anaesthesia to manage pain, measured preoperatively, with duration of opioid therapy following surgery
4. To characterize facial expressions occurring after receiving opioid therapy to manage pain following surgery and correlation with duration of opioid requirement after surgery.
5. To correlate emotional expressiveness, measured preoperatively, with changes observed with 3-D facial mapping technology

**Importance of Chronic Pain in the Community**

Chronic pain is a serious condition affecting 1 in 5 Australians.5 Aetiological factors for chronic pain have led to a recognition of the importance of severe acute pain after surgery *transitioning* to chronic post-surgical pain (CPSP).6,7 CPSP contributes to a significant burden of chronic pain, with 23% of all patients attending 10 chronic pain clinics  (n=5,130) in the UK attributing their pain to previous surgery.8 This has resulted in recent collaboration between the International Association for the Study of Pain (IASP) and the World Health Organization (WHO) to differentiate CPSP and trauma from other causes of chronic pain in the International Classification of Diseases (ICD-11) taxonomy to motivate research into early recognition and prevention of pain arising from these two specific aetiologies.9

**Transition of Acute Pain after Surgery to Chronic Post-surgical Pain**

Acute pain is almost ubiquitous after surgery. Fortunately, it can be controlled and mostly resolves within 1 week. It should not cause distress or limit postoperative recovery.10 For some patients, however, acute postoperative pain persists beyond the usual time of tissue healing and transitions into CPSP.11-15 The progression from acute to chronic pain following surgery involves sensitization of neuronal systems leading to permanent anatomical and physiological changes.7 The transition to a chronic pain state is more likely to occur in those with preoperative anxiety, depression, poor coping strategies and pain catastrophizing.16 This highlights the interrelationship between emotional factors and pain perception, and overt and likely subtle “facial signals” offering opportunities for detection and prognosis (see below).

The incidence of chronic post-surgical pain (CPSP) which is bad enough to cause significant functional impairment is approximately 10% of all surgeries.15 With more than 320 million people having surgery each year around the world this represents a vast potential for CPSP.17 As a result, CPSP is increasingly recognized as a public health problem, not only because of the discomfort, distress and disability it causes, but because past approaches to managing it have contributed significantly to the current “opioid crisis”.18 CPSP is far more common than most other postsurgical complications and has long-term consequences. The healthcare resource implications of CPSP should not be underestimated.

An understanding of the mechanisms responsible for transition of acute to chronic pain allow for specific targeting with analgesic therapies but the challenge remains to identify and treat patients susceptible to chronic pain secondary to surgery and trauma. Our project is focussed on the potential to intervene and initiate preventive treatment at a much earlier stage.

**Importance of Severe Pain in the Recovery Room**

Central nervous sensitisation following surgery or trauma leads to postoperative pain hypersensitivity due to lowered pain threshold in peripheral nociceptors and increased excitability of spinal neurons. Poor management of acute postoperative pain, as reflected by severe postoperative pain intensity in the first 24 hours following surgery,19 and at other times in the postoperative recovery phase,12 together with poor pain trajectory,20,21 show strong associations with CPSP. One study found that a 10% increase in pain within 24 hours of surgery resulted in a 30% increase in moderate to severe CPSP at 1 year, emphasising the need to target and manage early postoperative pain. In addition, functional impairment, as estimated by the Brief Pain Inventory22 increased with severity of CPSP, as do neuropathic characteristics.23

Earlier identification of those susceptible to severe acute pain may provide an opportunity for pain physicians to target sufferers with stronger analgesics such as ketamine or lignocaine infusion, gabapentinoids, and regional blockade in the immediate postoperative period. Unfortunately, there is no reliable and validated approach for assessing pain/nociception under general anaesthesia,24 so detection of pain is delayed until conscious is regained in the recovery room (leading to detrimental central sensitisation).

**Uncontrolled Pain in the ICU Setting**

Pain (nociception) and delirium are common in patients in the intensive care unit (ICU) setting.3 Better pain management has been demonstrated to improve outcomes such as decreased duration of mechanical ventilation and length of stay in the ICU,25,26 as well as reducing complications and hospital costs.24 However, at present there is a lack of adequate pain assessments in sedated critically ill patients.3 This hinders implementation of reliable evidence-based analgesic protocols that could further improve patient outcomes.27 A new approach would allow for a better systematic evaluation of pain by clinicians and allow for a better strategy for analgesic prescriptions with better flexibility in adjusting analgesic regimens to pain intensity.25

**Recognising Severe Pain in Patients who are Unconscious, have Delirium or Dementia**

Numerous studies have proposed various estimations using mainly blood pressure or heart rates as a measure of nociception used with novel multi-parametric index for estimation based upon a mixture of linear combination of nociception related physiological parameters and time derivatives with non-linear regression techniques.24,27 Current studies have been focusing on an automated non-invasive nociception monitor that directly assesses autonomic nervous system activity would be very useful for general anaesthesia, providing anaesthetists with feedback about the adequacy of antinociception.28 Monitors based on autonomic changes (heart rate variability, tachycardia, etc) are being marketed but have not proven to be very useful.24,29 Importantly, they are unreliable in disorders of consciousness,30 and have low sensitivity in intensive care patients.31 70% of patients in the Intensive Care setting are estimated to have undertreated pain.32

As stated by the IASP, clinicians must use pain assessment tools that are valid for all patients.27 In the ICU, self-reporting pain assessments remain the golden standard for pain evaluation.27,33,34 However, an obvious limitation to this method of pain evaluation is that the patient must be conscious to report the degree of nociception they are experiencing. In ICU, there are many situations where the patient is unable to communicate due to critical illness or if heavily sedated.27 Thus, problems lie in the inability to produce specific, reproducible and feasible monitoring tools.27

During emergence from anaesthesia patients typically regain their muscle tone before return of consciousness, but whether this related to subsequent severe pain or with cortical activation was unknown. Sleigh et al.35 recorded electroencephalographic (EEG) and electromyographic (EMG) activity from the forehead of 273 patients emerging from general anaesthesia after surgery and concurrently measured expired inhalational anaesthetic agent concentration (CeMAC) to determine CeMAC at time of EMG activation and return of consciousness. They found that the onset of EMG activation during emergence was not related to discernible muscle movement in half the patients. EMG activation could be modelled as two distinct processes; termed high- and low-CeMAC (occurring higher or lower than 0.07 CeMAC). Low-CeMAC activation was typically associated with simultaneous EMG activation and consciousness, and the presence of a laryngeal mask. In contrast, high-CeMAC EMG activation occurred independently of return of consciousness, and was not associated with severe postoperative pain, but was more common in the presence of a tracheal tube. Patients emerging from general anaesthesia with a tracheal tube in place are more likely to have an EMG activation at higher CeMAC concentrations. These activations are not associated with subsequent high-pain, nor with cortical arousal, as evidenced by continuing delta waves in the EEG. Conversely, patients emerging from general anaesthesia with a laryngeal mask demonstrate marked neural inertia-EMG activation occurs at a low CeMAC, and is closely temporally associated with return of consciousness.35{Hight, 2017 #38036}{Hight, 2017 #38036}{Hight, 2017 #38036}

Facial recognition of pain has been recently investigated in critically ill sedated intubated patients, where facial recognition examination during tracheal suctioning identified 5 pain related facial behaviours that accounted for 71% of variance in pain response.36 International guidelines recommend assessing pain with instruments based on behavioral parameters when critically ill patients are unable to self-report their pain level. As mentioned above self-reporting remains the gold standard. However, alternative methods have been developed to assess pain for unconscious patients. The most common is the Behavioral Pain Scale (BPS).3,4,33

Observation of facial behaviors has been suggested as a clinically useful means of assessing pain in the ICU population because of the unique facial expressions associated with pain compared with other affective states.33,37,38

Neuroimaging in humans have shown brain regions associated with emotions and motivation are activated during noxious stimulation and these regions may be altered in structure, activity or connectivity in people with pain.39 There is promising evidence of the usefulness of facial recognition technology for detection of pain in moderate to severe dementia, a common condition where pain is thought to be undertreated in approximately 67% but is not effectively communicated.40 A point of care electronic pain assessment tool has been recently developed and successfully trialed, showing excellent concurrent and discriminant validity and inter-rater reliability in this population.41

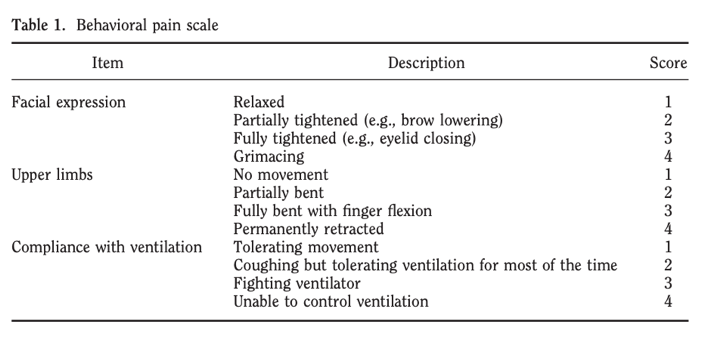
Pain in individuals with neurological disorders such as dementia is frequently under-recognised, underestimated, and undertreated.42 The inability to successfully communicate pain in severe dementia is a major barrier to effective treatment. The systematic study of facial expressions through a computerised system has found key features that are highly specific for pain, offering great potential for improved detection and treatment of pain in people with dementia.42

A potentially important application of facial recognition technology would be to provide for an earlier and more objective method of pain evaluation during emergence from general anaesthesia. There are some preliminary data, derived from adults with shoulder pain, showing automated facial recognition technology was more accurate than observer assessment.43 Earlier initial recognition of pain through behavioural detection may direct analgesic therapy to those who require it at an earlier stage during emergence from general anaesthesia and provide for more accurate ongoing vigilance to guide ongoing administration in the early postoperative period. This would ensure that promising therapies such as ketamine, gabapentinoids, lignocaine infusion and regional anaesthesia could be utilized in such a way as to maximize their potential to prevent CPSP.

Facial recognition technology for the detection of postoperative pain needs to be compared with accepted measures (such as a numeric rating scale) as these measures require a degree of interpretation and conceptualization that require a higher level of consciousness in the post-anaesthesia setting.

**Behavioral Pain Scale**

The BPS includes three behavioural indicators: facial expression, upper limb movements, and compliance with the ventilator.33 As mentioned above the facial expression is the most sensitive test with a score between 1 – 4 (Table 1).

1

**Relationship between Facial Expressions and Pain**

The facial action coding system (FACS) was developed to directly measure facial behavior,1,2 using palpation, knowledge of anatomy, videotapes, and photographs to determine how the contraction of each of the facial muscles changed the appearance of the face.1 From the study it defined 46 action units to correspond to each independent motion of the face.2 This was significant as it claimed to have universal human facial expressions in six different emotions; happiness, surprise, fear, anger, disgust, and sadness.1 This has been supported by many studies around the world,44 including studies showing strong correlations across cultures with interpretations of facial expressions.1,44,45

Pain behaviours are by definition observable and are socially reinforced towards pain behaviours as a way to ask for help or attention but can also be suppressed to avoid unpleasant events.45 Thus, judgment of pain in another person relies heavily on facial cues. Facial expressions have been divided into core action units (AU) with the characteristics including; brow lowering (corrugator: AU4), cheek raise and lid tighten (both parts of orbicularis oculi: AU6 and 7), nose wrinkle and upper lip raise (both parts of levator labii: AU9 and 10), and eye closing (AU43).3,45-47 Facial expression is the exception to this tendency, and excellent and detailed studies of facial expression of pain allow re-examination of the data using an evolutionary perspective.45 Frequency of pain patients facial action units (FAUs) were due to higher durations of pain from baseline at both the experimental and clinical pain level. This reinforced the theory towards chronic pain behaviours.45 What more, facial expressions of pain carry unique variance with the experience being interpreted through intensity, meaning, or degree of effect.48 A summary of FAUs that have been identified in numerous studies pain has been summarised by Prkachin et al.45

Although more than 6 facial action units has been reported with pain, there has been some inconsistency in the actions that have been identified. Prkachin also demonstrated that pain expressions relative to different types of pain sensations such as burn, electric shock, cuts etc., that the core of actions were strongly correlated across the different pain sensations.46 Including; movements of corrugator and orbicularis oculi, which lower the eye- brows, narrow the eye opening and raise the cheeks. Various other movements appear with some frequency, notably actions of levator labii superioris (which raise the upper lip, deepen the nasolabial furrow, or wrinkle the nose), eyelid closing and mouth opening. Eye closure was more likely during pain than baseline for electric shock, marginally more likely during cold and pressure and its duration was greater during pain than baseline for electric shock and pressure.46

**Technology to automate the recognition of FACS**

Studies support the use of facial expression as a pain indicator in critically ill patients.3 As demonstrated above, there is significant justification for why facial expressions are and deliver valuable data.47 Nociception/pain detection could be a continuous biological monitoring system that can be harnessed to improve well-being.37,45 Automated facial action coding could provide an objective measure of visual stimuli in such investigations of the neural substrates for the perception of facial expressions and could provide a behavioral measure of emotional state.2 An automated system should improve the reliability, precision, and temporal resolution of facial expressions2

**Facial expression measurement as a medical diagnostic tool**

Facial expression measurement from cameras provides an indicator of emotion activity that is less intrusive than EEG, EMG, autonomic nervous system measurements and brain imaging.2 An automated system allows facial expression measurements more widely accessible as a research tool in behavioural science and medicine and is therefore likely to provide an alternative measure of nociception.2

**Successful use of AI Facial Recognition technology in detecting pain**

Technology conversion has been unsurprisingly a success and has been already been used in the development of the electronic Pain Assessment Tool (ePAT), which uses a hybrid model: automated facial recognition and analysis, digitization, and clinical observations.34 The developed tool had a strong correlation of the ePAT with standard assessment of pain. This is because both scales have a similar construct and conceptual foundation in measuring aspects of pain-related behaviours.34 This validates the use of facial recognition technology to detect pain facial expressions.34

Previous attempts at automatic facial expression analysis systems have focused on either motion or surface gray levels. This differentiates human subjects who can recognize facial expressions from motion signals alone with recognition rates only above chance. Expression recognition improves with high temporal resolution videos. Studies have also integrated both surface gray levels and motion information.2 This has later evolved to a dynamic (sequence-base) or static (image-based).49

**Success/limitations in dynamic facial recognition methods in detecting emotional expressions.**

Currently, facial recognition can easily extract descriptive features from a face through a frame-by-frame motion in order to conduct facial expression analysis. By following the facial action units, we can localise each movement with intensity specified with a score from 0 being small to 1 being pronounced.49 Dynamic approaches generally outperform static approaches as it is more sensitive towards subtle expressions. The main problem for using dynamic facial expression analysis is the initial pre-processing system used to convert the input sequence into a useful representation.49 Current facial processing of emotional expressions is currently done through a mixture of manual search tasks, eye-movement monitoring, and dot com paradigm.50 However, there are three generalization challenges that are posed towards emotional expression capture:

1. Facial expressions displayed through spontaneous emotions usually display a wide range of movements as they may be expression a multitude of emotions. Therefore the representation must cover a wide range of expression intensities.45 This is best exemplified through two expressions; fright and surprise where they both share two mutual features; open mouth and wide-open eyes. Thus, facial emotional expressions, as a stimuli class, can be considered as rather complex and therefore visual working memory capacity for emotional expressions is expected to be low.47
2. Micro-expressions are a sub-class of subtle expressions in which small facial expressions are displayed and changed and can be for as short as 1/25 seconds.49
3. Learning a representation usually requires image sequences labelled with expressions and the applicability of the features learnt for a particular set of expressions may not extend to the recognition of other expressions.49

Subtle expressions are better recognised when using temporal variation with the sequence of frames.49 Recent studies have questioned the optimality of engineered dynamic representations, and aimed to learn representations from video volumes. One proposed architecture that comprised two networks; one that learned from facial appearances and the second to learn from facial data points.49 This method was found to improve performance of the engines.49 Dynamic approaches generally outperform static approaches as it is more sensitive towards subtle expressions.49 The main problem for dynamic facial expression analysis is the initial pre-processing system used to convert the input sequence into a useful representation.49 This will be minimised using 3-D Facial Mapping methods which is a dynamic approach which is incorporated in the Ayonix Facial Recognition engine, to detect facial expressions. This technology has already been used extensively in the security industry.51 One of the main challenges encountered by both features and appearance capture using facial recognition are based upon approaches that lie in the difficulties of handling harsh illumination conditions.51 Lighting models have also continuously demonstrated ability to collect better facial recognition features. As Almaddah et al51 demonstrated using a 2D model, statistical models were generally able to create a promising relighting and recognition process in order to better see different facial expressions. By using these a mixture of 3-D facial mapping techniques and lighting models, micro-facial expressions become detectable using sensitive image capturing equipment.

**Measurement of Acute Pain**

Clinical practice guidelines recommend frequent measurement of pain intensity in order to optimize treatment.52 Despite pain being acknowledged as a multi-dimensional experience, it is common for it to be assessed with one of several unidimensional scales. The most common is the visual analogue scale (VAS), which has become a standard measurement tool in pain research and clinical practice. But a reduction in a pain score of itself may not equate to an improvement in the patient’s experience.53-57

We therefore studied 224 patients after surgery and found that the minimal clinically important difference (MCID) of the pain VAS was 10 mm. That is, what minimal change in a pain VAS score would indicate a real change in a patient’s pain intensity?58,59 Analgesic interventions that provide a change of 10 for the 100-mm pain VAS signify a clinically important improvement or deterioration.

In addition, we have previously demonstrated that the VAS had linear scale properties in patients with acute pain after surgery,55,60 and concluded that the VAS score can be considered as ratio data for statistical analysis and interpretation.57 Patients with severe pain need immediate assessment and treatment, and such assessment should be quantifiable. We found that the VAS score is a linear measurement of severe acute pain.

**Non analgesic opioid effects**

Humans possess endogenous opioid systems comprising β endorphins, encephalins and dynorphins that circulate and interact with 4 subtypes of opioid receptors μ, δ, κ and opioid receptor like-1 receptors61. Interactions involving endogenous opioids and receptors located in the brain, spine and peripheral nervous system are thought to mediate analgesia, and behaviours that bring about reward, and control of emotion and stress62. Modulation of these endogenous opioid systems is often complicated by exogenous administration of opioids with the intention of controlling pain.

However, pain and pain behaviours are controlled through interactions involving many anatomical locations in the central nervous system other than those that purely influence pain (peripheral nociceptive neurones, dorsal horn and spinothalamic tract). These include the nucleas accumbens, and the ventral tegmental area that mediate emotion and addictive behaviours 63 and the periaqueductal grey matter, locus coeruleus, and the nucleas raphe magnus in the supraspinal centres that influence descending inhibitory pain modulation. 64

Behavioural effects of opioids involve research in animal models and humans that confirm influence of opioids in reducing aversiveness of experiences 65, 66, including pain 67 and may heighten the experience of pleasurable stimuli 68leading to the conclusion that opioids can be hedonistic 69. It comes as no surprise that these complex physiological interactions can create a scenario where pain relief and behavioural changes may be confused when exogenous opioids are administered to manage pain and set up the potential for addiction.

Given the potential for significant numbers of previously opioid naïve patients to continue to require opioids for long periods after recovery from surgery 70 and the known behavioural influences of opioids, the use of AI facial recognition may also provide a means of predicting susceptibility to opioid addiction.

**In Summary,** the detection of acute pain of severe intensity is of utmost clinical importance and is very difficult to detect in patients emerging from anaesthesia, in the elderly with delirium or dementia, or patients who are sedated/confused in the intensive care unit. Additionally the potential to predict opioid addiction potential through facial recognition may also be a useful clinical tool. Delayed or undertreated pain heavily weakens opportunities to achieve an optimal analgesic state and very likely increases the risk of CPSP and other chronic pain conditions. In addition, early recognition of sensitivity to addictive effects of opioids may direct analgesic treatments away from these potentially damaging agents at an early stage and play an important role in prevention of addiction. High-speed, 3-D facial recognition technology is an innovative solution.

**Methods**

This prospective study will evaluate adult patients having major surgery expected to cause postoperative pain of at least moderate intensity. The study will be conducted at the Alfred Hospital in Melbourne, a large university hospital with Statewide services in trauma, burns and lung transplantation. Ethics approval will be obtained, the study will be registered with the Australian New Zealand Clinical Trials Registry.

The following Departments will be contacted in relation to the study being conducted at The Alfred (Infection Control, Information Development Division), to ensure compliance with Hospital policy and appropriate use of resources are sought and appropriately reimbursed by researchers

Recruitment of patients for the trial will proceed as follows:

* The research assistant will consult the theatre operating schedule which can be accessed via password coded electronic record on the day prior to surgery. They will identify potential participants who meet inclusion criteria. Potential participants will be approached on the day of surgery.
* All interested patients will be approached in person by the research assistant for consent after arriving on day of surgery.
* The research assistant will provide more information by being available to answer questions in person. If the participant is interested in participating, they will then be provided with a patient information and consent form to read. If patients are happy to participate after they have discussed the project and read and understood the consent form, they can provide consent.
* Consent if agreed to by participant, will be obtained by the research assistant.

Any participants who develop complications as a result of participation in the study will have access to management with clinicians not directly involved with the study.

The goals of this study are to:

1. Determine whether there is a strong correlation between AI facial recognition patterns and the presence of pain prior to the patient waking fully from anaesthesia
2. See whether it is possible to correlate postoperative opioid requirement in those who were opioid naïve in the 2 weeks prior to surgery through AI facial recognition patterns after the administration of intravenous opioid prior to (where the patient has no pain) and following recovery (where patient may have postoperative pain) from surgery.

Patients will be eligible to participate in the study if they are:

* 18 -70 years of age,
* Scheduled for an elective surgical procedure requiring general anaesthesia,
* Requiring intravenous opioid as the main analgesic therapy for surgery.
* Anaesthetist happy to provide intravenous opioid prior to commencement of anaesthetic.
* Requiring intravenous opioid following surgery for a period greater than 48 hours.

Patients will be excluded if they have:

* Poor English comprehension
* Confusion impairing completion of the VAS and questionnaire (**note:** we plan to study those with dementia and delirium in the future, once we have validated the technology in this more select group of patients because we need to cross-validate with the VAS/NRS).
* Have been administered opioids for analgesia in the two weeks prior to surgery
* Have been diagnosed with opioid dependence disorder
* Have been diagnosed with current intravenous drug or illicit drug use

Baseline demographic and perioperative data will be collected on a paper case report form in re-identifiable form and transcribed onto an electronic database which is password coded. Paper documents and electronic data from the case report form information will be shredded after a storage period of 7 years.

* Age, sex, ASA, height, weight, BMI, ethnicity.
* Medical comorbidities (diabetes, hypertension, COPD, alcohol use, renal function, smoking, anxiety, depression, chronic pain), previous exposure to opioids prior to two weeks before surgery.
* Presence of pain prior to surgery, severity of pain prior to surgery.
* Type of surgery, duration of surgery (minutes.)

Patients will complete the following questionnaires preoperatively:

1. The Berkeley Expressivity Questionnaire (refer appendix 2)71. The Berkley Expressivity Questionnaire is a validated measure of emotional expressivity and may identify subgroups of patients who are more likely to benefit from AI facial recognition technology.
2. Opioid risk tool (refer appendix 1) The opioid risk tool questionnaire. The opioid risk tool is a validated measure of susceptibility to opioid addiction and may identify patients who are likely to require prolonged opioid therapy. 72 We will ask all questions in the opioid risk tool except the question regarding past history of sexual abuse as we feel that the unnecessary anxiety this might cause outweigh potential benefits.

Prior to surgery patients will have:

* A one-minute video of their face as a baseline.
* Have a second one-minute video of their face commencing one minute after they have received an intravenous injection of opioid prior to commencement of their general anaesthetic

At the completion of surgery but before emergence from general anaesthesia, quantitative monitoring will confirm restoration of neuromuscular function (because residual neuromuscular block would inhibit full facial expression 73) with time to achievement of neuromuscular recovery recorded in the datasheet.

Two traditional measures of pain intensity will be recorded, and each will be measured early after surgery as soon as clinicians feel they have can be accurately measured, with times of measurement recorded and subsequently correlated with facial technology:

1. *Behavioural Pain Scale* (for those unconscious or uncooperative) - We will use the BPS as an additional tool to assess unconscious patients.4 The BPS consists of the following three domains: “facial expression”, “upper limbs”, and “compliance with ventilation” Each domain is comprised of four descriptors, which generate a score from 1 to 4 points that increases with increasing pain. The total sum score of the instrument is generated from the three domains and can range from 3–12 points.4
2. *VAS* (at 30-60 min after emergence of anaesthesia, when conscious and cooperative) - A 100-mm VAS ranging from 0 (no pain) to 100 (very severe pain), will be used to measure pain intensity early after surgery.

In the Post Anaesthesia Care Unit (PACU) patients will have a one- minute recording of their face one minute after they receive their first intravenous opioid dose to treat pain as per the usual hospital protocol

Other parameters that will be measured include pain intensity in the PACU, opioid quantities administered in PACU, and duration of opioid requirement (in days) following surgery until all opioid analgesic therapy is ceased. Development of postoperative complications. Patients with postoperative complications will be excluded from assessment for opioid requirement as the complication may be associated with ongoing pain and may necessitate ongoing opioid therapy.

*Summary of 3-D Facial Mapping – Learning Dataset* *Processing:*

We will take a 1-minute video of the patient’s face;

1. As a reference reading before arrival in theatre
2. One minute after a preoperative intravenous dose of opioid is administered prior to induction of general anaesthesia
3. Immediately after surgery (wound closure and application of dressings), but before cessation of general anaesthesia, and a research nurse will assess the BPS of the patient.
4. In the Post Anaesthesia Care Unit 1 minute after the first intravenous dose of opioid administered for analgesia is completed

The images will be added into the database with the proposed system architecture, using 3-D Facial Mapping techniques with highly sensitive camera equipment that is able to capture micro-facial expressions. Paper based data will be re-identifiable, and stored in a locked cabinet only accessible by the researchers. Details of the data processing is as follows:

Facial data extraction - the video will be uploaded onto a secure database, which is password coded and only accessible by the researchers. The video database will be managed by Strong Room technologies and will not involve the Alfred Hospital redcap system.

The database details are: Microsoft Azure + Microsoft SQL Server with APP considerations (with the cloud server to ensure the data is physically stored in Australia).

Researchers from Strong Room technologies will utilize the following approved software to manage the data:

Microsoft Azure

Hardware’s internal camera

USB (encrypted + password protected)

The measures taken to ensure security of data will include:

Addressing Brute Force hacking:

- Set-up of limited password attempts

- Username will be known by each individual

- Passwords will be set to a 8 character minimum requirement

- Will recommend each individual to think of a word such as walmart where the password will then be W&Lm@rt

- Passwords will be centrally monitored from a desktop computer located in a secure facility owned by Strong Room

Ransomware

- Individuals will be issued with unique hardware for the purpose of this study

- Strong Room engineers will instruct upon the correct settings and programs

- Research staff are instructed not to open any emails except those from within the recognised emails

- Emails will be especially created for the purpose of the research

Eavesdropping

- Only known emails and applications will be used

- Strictly no personal email or social media accounts will be uploaded onto the devices

Data Compromise

- Data will have end-to-end encryption including USB’s

- Data will remain encrypted on a cloud database and decrypted with proper login

Data Handling

- After the data has been processed and the individuals no longer needed to be contacted, all personal information including the following will be destroyed with the exception of images that may be used for future internal research for up to 7 years:

- Name

- Address

- Phone Number

- Medical Number / Social Security Number / Any other number

Data Transfer

- Data transfer from the cameras must be done ​daily ​ and immediately deleted.

- All data from cameras will be transferred onto the approved hardware and uploaded onto approved hardware.

- USB will be ensured to be wiped after every data transfer.

- USB will be held on a necklace to ensure that they are not lost by research assistants

Storage Security

- HIPAA requirements will be set upon the data with security features including: - Encryption as specified above

- Database will be separate both physically and digitally from any other sources

- Will use Microsoft as a vendor (Microsoft Azure) which has many use cases with handling sensitive information

Human Error - All hardware must be accounted for, at a weekly meeting.

- Centrally monitored desktop from a secure position owned by Strong Room will be the administrator with capabilities of a “force log-out” feature towards each hardware.

Cybersecurity protocols will be reviewed on a quarterly basis.

The technical team will then:

1. Process the postoperative video taken prior to waking and cut frame by frame into images from which they will be organised into the corresponding BPS score (from 1 = facial expressions with no pain, to 4 = extreme pain).
2. Process the preoperative video following opioid administration and cut frame by frame into images from which they will be organised into corresponding groupings of duration of postoperative opioid requirement.
3. Process the postoperative video following opioid administration in the post anaesthesia care unit and cut frame by frame into images from which they will be organised into corresponding groupings of duration of postoperative opioid requirement.

Processing of the videos will proceed as follows:

1. Face detection - using multiple algorithms to detect facial landmarks in an image, which essentially detects the face with basic human features such as eyes, nose, and mouth.
2. Face tracker - once a face is detected, the face tracker phase is initialized. This then detects the best quality image taken with the score selection and then initiates an analysis of the image:
3. The tracker evaluates frames and decides the best frontal face checking
4. Face angle, face expression, shadow on face surface and face pixel intensity
5. Face tracker simultaneously judges for the best face to get the highest facial recognition score and lowest error.
6. Face pre-processing - This phase includes detection of faces from a given image and extracts features for each face, attributing gender, age and other features for each face. It is important to emphasize that, in this stage, individual (patient) faces begin to be processed.
7. 3-D Construction - A 3-D module takes each face and constructs a 3-D model from a single face image. The model once again checks for basic human face features (e.g. nose), and generates a 3-D model of a face in its entirety. After finding 37 basic points, the face mask is generated with more than 200 landmark points, fixing the mask on the face surface. This involves rotating the face to a frontal position, removing noise and strong lighting effects. Our 3-D module prepares faces to the perfect condition before recognition. Therefore, in our study we will be establish the most ideal conditions as possible.
8. Feature extraction - Ensuring correctness and uniqueness in invariant features is the most important duty for the feature extraction module. This extracts all features from the face surface, including all visible features such as eye-nose-mouth distance information, eye-nose depth, correlation of face landmark points, unique features of face, and shape information (eye shape, nose shape, mouth shape, face boundary etc). The face extraction phase converts image information into a digital binary form.
9. Face verification - Compares the face features against preloaded face features. During verification, binary data is compared to binary data in the memory.
10. Product concept of face diagnosis - This stage will involve reconfiguring the database stage to start detecting facial micro-facial expressions of pain and using pain landmarks as outlined in the FACS.46
11. New structure of face recognition – Here we will “train” patient video data to create a database, a dataset generated from patient faces. Figure 1 demonstrates how facial recognition interacts with different databases.

Postoperative follow up of patients in hospital

We will follow patients while they remain in hospital and measure need for ongoing opioid requirement and opioid quantity and convert to oral morphine equivalent. We will also measure pain intensity at rest and with movement and common opioid related side effects (itch,nausea/vomiting, sedation).

Other outcome measures will include Quality of Recovery (using the QoR-15 scale) 74,75 at 4 and 24 hours.

Postoperative follow up of patients after discharge from hospital

After discharge patients will be contacted by researchers by phone. Contact will continue until patients cease their opioid medication. The plan for phone contact will involve a schedule of daily contact for up to 3 days (if the patient continues to take opioid) then weekly if required. The phone script for a typical review call will include:

* Ringing patient from hospital landline
* Confirming patient identification (name)
* Enquiring whether patient has continued opioid
* If continuing opioid then check type and quantity of opioid
* Enquire whether there are problems with the operation
* If problems are reported then researcher can organise immediate review of patent by surgeon involved in their care
* If patient is continuing opioid, inform patient that contact will be established again as per the schedule to review opioid dose.
* Enquire whether patient has any questions about the study

**COVID-19 Precautions**

Precautions will be exercised in order to minimize infection spread of COVID-19 and other microorganisms.

Researchers will need to exercise infection control to minimise infection through appropriate distancing, use of personal protective equipment and sterilization as follows:

* Researchers will need to ensure that they do not come into direct contact with patients and continue to practice safe spacing (at least 1.5 metre distancing from patient), whether approaching on the ward to seek consent or in the operating theatre.
* Researchers should wear personal protective equipment as appropriate.
* It may be necessary to seek consent via verbal means to minimise sharing of paper and stationary when seeking written consent.
* The video device will have to be sterilized by cleaning with an alcoholic preparation of minimum concentration of 60% in between uses and be kept at a distance greater than 1.5 metres from the patient when in use.

**Statistical Analysis**

We cannot reliably estimate a required sample size for this study because of the uncertain pain intensity and correlations. We plan to enrol 120 subjects (60 development set, 60 validation set) to allow additional exploratory and subgroup testing.

Descriptive data will be reported as mean (SD), median (IQR), and number (%) unless otherwise specified. Selected results will be reported with 95% confidence intervals. Associations between pain scores, and facial data and opioid consumption and opioid duration and facial data will be analysed using Pearson correlation coefficient; specific agreement analyses will use the intraclass correlation coefficient. Regression analysis will be used to demonstrate the difference between the pain scores with the independent level as the time or movement in facial expressions and the dependent variable used as the pain scores. All statistical analyses will be performed using SPSS for Windows V23.0 (SPSS Australasia Ltd., Sydney). A P value of <0.05 will be considered significant; no correction will be made for multiple comparisons.

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