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SMART PAIN ASSESSMENT TOOL FOR CRITICALLY ILL PATIENTS UNABLE TO COMMUNICATE

Early stage development of a medical device

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To my daughters Lilja, Viola and Linnea

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ABSTRACT

Critically ill patients often experience pain during their treatment but due to patients' lowered ability to communicate, pain assessment may be challenging. The aim of the study was to develop the concept of the Smart Pain Assessment tool based on the Internet of Things technology for critically ill patients who are unable to communicate their pain.

The study describes two phases of the early stage development of the Smart Pain Assessment tool in a medical device development framework. The initiation Phase I consists of a scoping review, conducted to explore the potentiality of the Internet of Things technology in basic nursing care. In the formulation Phase II, the prototype of the Smart Pain Assessment tool was tested and the concept was evaluated for feasibility. The prototype was tested with healthy participants (n=31) during experimental pain, measuring pain-related physiological variables and activity of five facial muscles. The variables were combined using machine learning to create a model for pain prediction. The feasibility of the concept was evaluated in focus group interviews with critical care nurses (n=20) as potential users of the device.

The literature review suggests that the development of Internet of Things -based innovations in basic nursing care is diverse but still in its early stages. The prototype was able to identify experimental pain and classify its intensity as mild or moderate/severe with 83% accuracy. In addition, three of the five facial muscles tested were recognised to provide the most pain-related information. According to critical care nurses, the Smart Pain Assessment tool could be used to ensure pain assessment, but it needs to be integrated into an existing patient monitoring and information system, and the reliability of the data provided by the device needs to be assessable for nurses.

Based on the results of this study, detecting and classifying experimental pains intensity automatically using an Internet of Things -based device is possible. The prototype of the device should be further developed and tested in clinical trials, involving the users at each stage of the development to ensure clinical relevance and a user-centric design.

KEYWORDS: Critically ill patient, critical care, intensive care unit, Internet of Things, machine learning, medical device, pain assessment

TURUN YLIOPISTO
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TIIVISTELMÄ

Kriittisesti sairaat potilaat kokevat usein kipua hoidon aikana, mutta potilaiden kivun arviointi on haastavaa tilanteissa, joissa potilaan kyky kommunikoida on alentunut. Tutkimuksen tavoitteena oli kehittää toimintakonsepti esineiden internet -teknologiaan perustuvalle Älykkäälle kipumittarille, joka on suunniteltu kriittisesti sairaille potilaille, jotka eivät kykene kommunikoimaan kivustaan.

Tutkimuksessa kuvataan Älykkään kipumittarin varhaisia kehitysvaiheita lääkinnällisen laitteen kehitysprosessin mukaisesti. Aloitusvaiheessa I toteutettiin kartoittava kirjallisuuskatsaus, jossa selvitettiin esineiden internet -teknologian mahdollisuuksia perushoidossa. Muotoiluvaiheessa II testattiin laitteen prototyyppiä ja arvioitiin laitteen toimintakonseptin toteutettavuutta. Prototyypin testaukseen osallistui terveitä koehenkilöitä (n=31), joille tuotettiin kipua. Kipualtistuksen aikana mitattiin kipuun liittyviä fysiologisia muuttujia ja viiden kasvolihaksen aktivoitumista. Muuttujat yhdistettiin koneoppimismenetelmällä kivun ennustemalliksi. Lisäksi teho-osastolla työskentelevät sairaanhoitajat (n=20) arvioivat fokusryhmähaastatteluissa laitteen toimintakonseptin toteutettavuutta.

Kirjallisuuskatsauksen tuloksista käy ilmi, että esineiden internetiin perustuvien innovaatioiden kehittäminen perushoidon tukemiseen on monipuolista mutta se on vielä alkuvaiheessa. Älykkään kipumittarin prototyyppi osoittautui lupaavaksi kokeellisen kivun tunnistamisessa ja sen voimakkuuden luokittelussa, saavuttaen 83 %:n tarkkuuden kivun luokittelussa lievään tai kohtalaiseen/voimakkaaseen. Lisäksi todettiin, että viidestä mitatusta kasvolihaksesta kolme antoi merkittävintä tietoa kivun tunnistamiseen ja voimakkuuteen liittyen. Sairaanhoitajat näkivät potentiaalia Älykkään kipumittarin käytössä potilaiden kivun arvioinnissa teho-osastolla. Laite tulisi kuitenkin integroida käytössä olevaan potilastietojärjestelmään, ja laitteen tuottamien tietojen luotettavuus tulisi olla hoitajien arvioitavissa.

Tulosten perusteella esineiden internet -teknologiaan perustuvan laitteen avulla on mahdollista tunnistaa ja luokitella kokeellisen kivun voimakkuutta automaattisesti. Laitteen prototyyppiä tulee jatkokehittää ja testata kliinisissä tutkimuksissa. Tulevat käyttäjät tulee ottaa mukaan jokaiseen kehitysvaiheeseen laitteen kliinisen merkityksen ja käyttäjälähtöisen muotoilun varmistamiseksi.

AVAINSANAT: Esineiden internet, kivun arviointi, kriittisesti sairas potilas, koneoppiminen, lääkinnällinen laite, tehohoitotyö, teho-osasto

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Abbreviations

ACM DL	Association for Computing Machinery Digital Library
Ag/AgCl	Silver/silver chloride reference eletrode
AI	Artificial intelligence
ANI	Analgesia Nociception Index
ANN	Artificial neural network
AU	Action unit in Facial Action Coding System
AUC	Area under the ROC curve
BIS	Bispectral Index
BOT	Behavior Assessment Tool
BPS	Behavioral Pain Scale
BPAT	Behavioral Pain Assessment Tool
BPS-NI	Behavioral Pain Scale for Non-Intubated
BPAT	Behavior Pain Assessment Tool
CPOT	Critical-care Pain Observation Tool
DB	Diastolic blood pressure
EDA	Electrodermal activity
ECG	Electrocardiography
EMG	Electromyography
EU	European Union
FACS	Facial Action Coding System
FDA	United State Food and Drug Administration
FPT	Faces Pain Thermometer
GSR	Galvanic skin response
HR	Heart rate
IASP	International Association for the Study of Pain
ICU	Intensive care unit
IoT	Internet of Things
ISO	International Organization for Standardization
k-NN	k-Nearest Neighbor
MAP	Mean arterial pressure
MDR	Medical Devices Regulation

NOL	Nociception Level Index
NPAT	Nonverbal Pain Assessment Tool
NRS	Numeric Rating Scale
NVPS-I	Nonverbal Pain Scale initial
NVPS-R	Nonverbal Pain Scale revised
PAD	Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the ICU
PADIS	Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU
P.A.I.N.	Pain Assessment and Intervention Notation
RFID	Radio frequency identification
RMS	Root mean square
ROC	Receiver operating characteristic
RR	Respiratory rate
SaO2	Arterial oxygen saturation
SBP	Systolic blood pressure
SCA	Skin conductance algesimeter
TENS	Transcutaneous electrical nerve stimulation
TPR	True positive rate
VAS	Visual Analog Scale
VNS	Visual Numeric Scale
WL	Wave length
WLAN	Wireless local area network

List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Mieronkoski R, Azimi I, Rahmani A, Aantaa R, Terävä V, Liljeberg P & Salanterä S. Internet of Things for Basic Nursing Care – A Scoping Review. *International Journal of Nursing Studies,* 2017; 69(2):78–90.

II Jiang M, Mieronkoski R, Syrjälä E, Terävä V, Anzanpour A, Rahmani A.M, Salanterä S, Aantaa R, Hagelberg N & Liljeberg P. Acute pain intensity monitoring with the classification of multiple physiological parameters. *Journal of Clinical Monitoring and Computing*, 2019; 33(3):493–507.

III Mieronkoski R, Syrjälä E, Jiang M, Rahmani A, Pahikkala T, Liljeberg P & Salanterä S. Developing a pain intensity prediction model using facial expression: A feasibility study with electromyography. *PloS ONE*, 2020; 15(7): e0235545.

IV Rosio R (former Mieronkoski), Matinolli H-M, Niela-Vilén H, Liljeberg P & Salanterä S. A qualitative study of critical care nurses' perceptions on the use of smart technology for pain assessment in the intensive care unit. A manuscript.

1 Introduction

The sickest patients, who are having acute life-threatening organ dysfunction, are treated in intensive care units (ICUs) (Marshall et al., 2017). These patients are often suffering from multiple interconnected distressing and unpleasant physical and psychological symptoms such as pain, agitation, anxiety, confusion, difficulties to breath, tiredness and thirst (Puntillo et al., 2010; Rotondi et al., 2002). Pain in critically ill patients is often a result of individual characteristics, interventions including operations and daily care procedures, and underlying disease processes (Olausson el al., 2013; Puntillo et al., 2010). The ability to express extent of pain verbally or by other voluntary means is often limited in critically ill patients, especially during mechanical ventilation.

The treatment of critically ill patients should be based on the lightest possible sedation and effective analgesia. In this way, the primary goal of care could be achieved: patients should be comfortable and calm and be able to cooperate with healthcare personnel and family members. (Vincent et al., 2016.) Achieving this goal requires systematic and effective pain and sedation management. To ensure adequate pain management, it is necessary to assess pain, identify patients who need interventions and evaluate the effectiveness of pain management. Pain is a subjective multidimensional phenomenon and the "gold-standard" in pain assessment relies on self-reporting. In situations where the patient's ability to communicate is impaired, pain assessment remains a challenge. Currently, there is no valid and reliable objective means to assess pain (Herr et al., 2019a). Pain can be assessed by changes in two different categories that can be partly quantified in cases where self-reporting is not available. The first relates to changes in the central nervous system. The second is the behavioural changes associated with pain including withdrawal or avoidance, and expressive acts such as vocalising or grimacing. (Hadjistavropoulos & Craig, 2002.)

Technology is an integral part of care for critically ill patients. Recent technological advances have enabled the use of artificial intelligence (AI) in healthcare. However, in nursing the implementation of AI enabled innovations is still uncommon. Symptom monitoring and management are areas specific to nursing that could be strengthened by the application of AI. The Internet of Things is a smart

technology often supported by AI that has the ability to connect to a network to share and interact with other devices or human users (Silva et al., 2018). The aim of the study was to develop a concept of the Smart Pain Assessment tool, an automated pain detection method based on the Internet of Things technology. The ultimate goal is to develop a clinically useful medical device for the ICU environment enabling continuous and automated detection of acute pain in critically ill patients unable to self-report their pain.

2 Review of the Literature

The literature review is twofold; first, the current evidence in pain assessment methods in critically ill patients are introduced. Secondly, the current stage of research in automated pain detection methods is reviewed. Using the information from these two elements, the need and the theoretical basis is formulated for the innovation of Smart Pain Assessment tool.

The literature search was done in three phases using the databases PubMed (Medline), CINAHL, and the Web of Science. (Appendix 1.) The topics of the searches were 1) pain assessment in critically ill patients, 2) facial expression of pain, and 3) automated pain detection. An additional search for facial expressions of pain was conducted due to the limited findings from the previous research in the area of facial expressions among critically ill patients. The literature searches were supplemented by reviewing the reference lists of the chosen articles and suggestions from the refence management system Mendeley. In addition, relevant articles were used to define the concepts of the study.

Studies with the following inclusion and exclusion criteria were chosen for the review. (Appendix 2.) Studies covering the research on pain assessment in critically ill patients were included in the review with the main focus in the methods of pain assessment. The literature search was limited to adult patients and those studies describing automated pain detection methods were limited to acute pain and adults. The research on chronic pain and studies related to specific diagnoses (e.g. low back pain) and syndromes associate with pain (e.g. fibromyalgia) were excluded. Articles describing only the development of or exploration of methods without a clear clinical context were also excluded.

2.1 Pain in critically ill patients

Pain is one of the major stressors that patients experience whilst being treated in ICUs (Zengin et al., 2020; Azizi-Fini et al., 2017). Pain is defined according to the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage" (Raja et al., 2020). The definition is followed by notes that emphasise the subjective and multimodal nature of pain, and that the verbal expression of pain is not the only behaviour through which it can be expressed (Raja et al., 2020). This subjectivity is stressed in the clinical definition "Pain is whatever the experiencing person says it is, existing whenever he/she says it does" (McCaffery, 1968).

The term nociception describes the physiological process by which noxious stimuli are encoded and processed. Nociception and pain should not be confused, as they can occur together or on their own. (Loeser & Treede, 2008.) The pain processing involves several stages: transduction, transmission, modulation, perception and interpretation. In the transduction, specialised sensory neurons known as nociceptors located in skin, joints, muscles, and internal organs, become activated. (Garland, 2012.) These nociceptors can be triggered by various stimuli, including mechanical pressure, temperature (heat/cold), or exposure to chemicals. Nociceptors are connected to thin myelinated Aδ fibers and unmyelinated C-fibers, which ultimately terminate in the spinal cord's dorsal horn. Nociceptors can be roughly categorised into two classes: Aδ fibers, responsible for transmitting sharp and fast pain signals, and C-fibers, responsible for conveying slow, persistent, and dull pain signals. (Garland, 2012; Reddy et al., 2012.) During the transmission, the nerve impulses generated by these sensory nerve terminals travel from the periphery to the spinal cord. From there, these impulses are conveyed along nerve pathways through the spinal cord and brainstem, ultimately reaching various regions of the brain, including the thalamus and somatosensory cortex. Modulation introduces variability into the transmission of pain signals, which can differ both among individuals and within the same individual at different times. The descending pain modulatory system has both pro-nociceptive effects to facilitate nociception, and anti-nociceptive to inhibit nociception. Pain perception occurs in the brain when these signals are processed. (Garland, 2012.) The experience of pain is inherently individual, influenced by cognitive and social factors (Raja et al., 2020). Pain represents an individual's unique interpretation of pain signals based on their personal experiences, emotions, and expectations.

As emphasised in the definition of pain, the inability to express pain verbally does not mean that it is not possible for a person to experience pain (Raja et al., 2020). Most patients in ICU are unable to self-report their symptoms because of their clinical conditions, altered consciousness levels or the use of sedatives or

neuromuscular blocking agents (Burry et al., 2014; Bennett & Hurford, 2011). Being intubated during mechanical ventilation is one of the main reasons for not being able to communicate verbally (Guttormson et al., 2015). The use of sedatives does not eliminate the possibility of pain, on the contrary, sedatives can in some cases even increase pain perception (Frölich et al., 2013). Agitation and anxiety are often associated with critical illness as distressing condition, inability to communicate, being away from the family and being mechanically ventilated (Tate et al., 2012). Experiencing pain also predisposes patients to delirium, which is often an undiagnosed syndrome of disturbance in consciousness and a change in cognition (Cavallazzi et al., 2012). Delirium may increase and confuse the assessment of the of other interconnected unpleasant symptoms like pain (Reade & Finfer, 2014). The critical care nurses may underestimate pain among the other unpleasant symptoms in mechanically ventilated, sedated critically ill patients (Randen et al., 2013).

The study of Vincent et al. (2016) divides the pain in critically ill patients into four categories: 1) pre-existing persistent pain 2) acute pain related to an ongoing disease including post-operative, visceral and trauma pain, 3) intermittent acute pain associated with care procedures, and 4) continuous pain/discomfort related treatment caused by mechanical ventilation or immobilisation/stiffness (Vincent et al., 2016). This classification presents the heterogeneity of pain in its duration, aetiology and pathophysiology.

2.1.1 Pain prevalence and effects of untreated pain

The prevalence of pain in critically ill patients varies across studies; it has been suggested that 50−77% of patients suffer from untreated pain, depending on the study population and pain assessment methods (Sigakis & Bittner, 2015; al Sutari et al., 2014). Fortunately, there may have been some advances in pain rates. In the contrast to the study of Gélinas et al. (2007) where 77.4% of 93 patients recalled having pain during the treatment in an ICU, a recent study by Olsen et al. (2021) reported that only 10% of the assessed critically ill patients were in pain when at rest and 27% had procedural pain after implementing a pain management protocol.

Critically ill patients commonly experience mild to severe acute pain during routine invasive and non-invasive procedures. Endotracheal suctioning and turning/repositioning are often rated as the most painful procedures (Ayasrah, 2016; Arroyo-Novoa et al., 2008; Gélinas, 2007; Puntillo et al., 2001). Chest tube and wound drain removal and arterial line insertion are also among the most painful procedures (Puntillo et al., 2014, 2018). Procedures connected to early rehabilitation, like mobilisation, deep breathing and coughing exercises, might cause pain (Puntillo et al., 2014; Siffleet et al., 2007). There is no consensus on painfulness on some of the daily procedures and even harmless daily care procedures may cause pain. For

example, oral care has been used in studies as a painless control measure (non-nociceptive procedure) in critically ill patients (Ayasrah, 2016) but in a study on oral care in critically ill patients, the patients found oral procedures to be painful, uncomfortable and emotionally distressing (Dale et al., 2020). In addition, dressing change has been used as non-nociceptive procedure (Ayasrah, 2016) even if it is reported as painful procedure in some studies (Puntillo et al., 2018). Non-invasive blood pressure cuff inflation and eye care are examples of painless procedures used in studies (Ayasrah 2016, al Sutari et al., 2014).

Several risk for experiencing higher pain intensity during ICU care have been identified associated with patient characteristics and care. These risks include young age (Ayasrah, 2016; al Sutari et al., 2014) non-white ethnicity (Arroyo-Novoa et al., 2008), specific care procedures (al Sutari et al., 2014; Puntillo et al., 2014), administration of opioids specifically for the procedure, pre-procedural pain or distress, most severe pain experienced on the same day, and procedure performed by individuals other than nurses (Puntillo et al., 2014).The procedures that are experienced as most painful in critical care varies among age groups; for adult critically ill patients turning is one of the most painful and distressing procedure, whereas for adolescents it was wound care (Puntillo et al., 2001). Moreover, pain before ICU admission is one of the risk factors identified as causing persistent pain to be associated with the ICU treatment after the discharge (Mäkinen et al., 2020; Kemp et al., 2019).

Untreated pain or suboptimal pain management in critically ill patients may lead to several adverse events, poor clinical outcomes and causes human suffering. Acute pain activates the sympathetic nervous system which leads to an increase in stress hormones (Barr et al., 2013). In critically ill patients, this may lead to vasoconstriction, increases oxygen demand, alters glycaemic regulation and impairs immune function (Sigakis & Bittner, 2015). Adverse events associated with untreated pain may be fatal to critically ill patients as higher pain intensity has been associated with increased mortality rate among mechanically ventilated patients (Yamashita et al., 2017). Untreated pain is also associated with higher rates of agitation (Bennett & Hurford, 2011). Untreated pain during intensive care also has long-term consequences: long-term pain rates were observed to range from 14% to 77% in an investigation into pain one year after discharge from ICU (Kemp et al., 2019). Furthermore, adverse events and poor clinical outcomes associated with untreated pain may lead to post-intensive care syndrome including persistent and severe physical, cognitive, and psychological deficits (Rawal et al., 2017). While some factors associated with chronic pain after intensive care have been identified, the underlying mechanisms have remained unclear and require further investigation (Kemp et al., 2019).

2.1.2 Clinical guidelines for pain management

The ABCDEF Bundle in Critical Care is an evidence-based guideline to optimize the outcomes and recovery of ICU patients (Marra et al., 2017). The bundle includes six components of patient care: **A**ssess, Prevent, and Manage Pain, **B**oth Spontaneous Awakening Trials and Spontaneous Breathing Trials, **C**hoice of analgesia and sedation, **D**elirium: Assess, Prevent, and Manage, **E**arly mobility and Exercise, and **F**amily engagement and empowerment. The pain assessment, prevention and management are guided by the Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in an Intensive Care Unit (PAD guideline) created by the Society of Critical Care Medicine (Barr et al., 2013). The PAD guideline was updated by an expert group in 2018 leading to The Pain, Agitation/sedation, Delirium, Immobility, and Sleep disruption (PADIS) guidelines. An update on immobility and sleep disturbance was added to the recommendations, as these aspects were found to influence the experience of pain, the use of sedation and the incidence of delirium (Delgado, 2020; Devlin et al., 2018).

The American Society for Pain Management Nursing has published a statement position and clinical practice recommendations for patients unable to self-report (Herr et al., 2019a; Herr et al., 2019b). For the pain assessment of critically ill unconscious patients, the following five-step protocol is proposed: 1) search for potential causes of pain, including known painful interventions and procedures 2) attempt to obtain the patient's self-report of pain 3) observe the patient for pain related behaviour 4) ask proxy about pain and behaviour/activity changes 5) attempt an analgesic trial (Herr et al., 2019a).

2.2 Pain assessment in critically ill patients

Systematic pain assessment is associated with improved treatment outcomes in critically ill patients; these include reduced duration of mechanical ventilation, length of stay in intensive care and reduced complications (Georgiou et al., 2015). Pain assessment has a major role in effective pain management in critically ill patients as pain assessment is associated with lower pain intensities, incidence of pain episodes (Georgiou et al., 2020), and increases the use of analgesic administration (Phillips et al., 2019).

Self-report of pain is the "gold standard" of pain assessment in critically ill patients, and it is used in patients who are able to communicate (Herr et al., 2019a). Pain should be assessed using a validated pain scale, rather than with a yes/no question. This will allow the intensity, type and location of pain to be accurately determined and the response to pain treatment to be assessed. (Chanques et al., 2010.) Pain assessment tools validated for critically ill patients who are able to self-

report are the numeric rating scale (NRS), verbal rating scale (VRS) and visual assessment scale for pain (VAS). The most feasible and discriminative tool is a horizontal 11-point NRS scale in a visually enlarged laminated form. (Chanques et al., 2010.) For critically ill patients unable to communicate, the literature especially promotes the use of three observational tools: the Behavioral Pain Scale (BPS), the Behavioral Pain Scale for non-intubated (BPS-NI), and the Critical Care Pain Observation Tool (CPOT) as they have been found to be valid and reliable in various settings and countries (Gélinas et al., 2019b; Pudas-Tähkä & Salanterä, 2018). In addition, the PADIS guidelines recommend the use these pain assessment tools (Devlin et al., 2018). In practice, self-reporting and observational measures are used interchangeably to assess pain, as the mental state of patients varies. The correlation between of self-reported and observational pain assessment methods is still questionable: when testing five observational pain measures against patient self-reported pain ratings, all the tested pain scales had moderate to high correlations with the patient's self-report during suctioning (Arif-Rahu et al., 2015). However, the study by Bouajram et al. (2020) found that the results between behavioural pain scales and self-reports may not correlate and current validated behavioural pain scales may not provide an accurate interpretation of self-reported pain in critically ill patients.

The implementation of published guidelines on pain assessment in critically ill patients is inconsistent (Hamdan et al., 2022; Hamdan, 2019; Kemp et al., 2017). For example, in the study conducted in 45 ICUs in the United Kingdom, only two ICUs used validated observational pain assessment tools and one fifth of the patients received no pain assessment at all during the 24-hour study period (Kemp et al., 2017). Moreover, it was found that while using the observational pain assessment tools, the nurses might not choose the most valid and reliable tools intended for the particular patient group (Hamdan, 2019). Several barriers have identified to pain assessment and management in ICUs. These include a heavy workload, patient related issues including patient instability, the use of sedation, and an inability to communicate (Hamdan et al., 2022).

2.2.1 Observational pain assessment tools

The observational tools are mainly based on observation of the various actions associated with pain behaviour: paralinguistic vocalisation, facial expression, body posture, movement rigidity, and behaviour of escape and avoidance. These signs are often in the automatic, nondeliberate domains and beyond purposeful communication. (Hadjistavropoulos & Craig, 2002.) Over the past ten years, several systematic reviews have introduced and explored the psychometric properties of observational pain assessment tools targeted to critically ill patients who are unable

to communicate (Gélinas et al., 2019b; Gélinas et al., 2013; Stites, 2013). The most recent systematic review (Gélinas et al., 2019b) updated the previous work on the psychometric properties on the of the pain assessment tool. They found nine pain assessment tools originally developed for the critical care; the Behavior Assessment Tool (BOT) (Puntillo et al., 2004), the Behavioral Pain Assessment Tool (BPAT) (Devlin et al., 2018), the Behavioral Pain Scale (BPS) (Payen et al., 2001), the Behavioral Pain Scale Non-intubated (BPS-NI) (Chanques et al., 2009), the Critical-care Pain Observational Tool (CPOT) (Gélinas et al., 2006), the Pain Assessment and Intervention Notation (P.A.I.N.) (Puntillo et al., 1997), the Nonverbal Pain Assessment Tool (NPAT) (Klein et al., 2010), the Nonverbal Pain Scale (initial) (NVPS-I) (Odhner et al., 2003) and the Nonverbal Pain Scale (revised) (NVPS-R) (Kabes et al., 2009). (Table 1.)

There are both behavioural and physiological domains in the observational pain assessment tools. The most common behavioural domains are the facial expression (included in 9/9 of the pain assessment tools), movements of the body or upper extremes (8/9), vocalisation (5/9), guarding (3/9), muscle tension (3/9), and posture (2/9). Three of the nine observational pain assessment tools also include physiological domains in addition to the behavioural domains. The P.A.I.N. tool and the Nonverbal Pain Scale (NVPS-I and NVPS-R), both contain several physiological domains including the evaluation of heart rate, blood pressure, respiration, perspiration, and pallor, and the NVPS-I also includes the domains of skin temperature, pupil dilation, and flushing. The scoring system varies from one assessment tool to another, i.e. by observing the items either on a simple present/absent scale (e.g. BOT, BPAT) or more accurately describing the degree (e.g. CPOT, BPS).

The BPS, BPS-NI, and CPOT have the best psychometric properties and the largest pool for evidence among the evaluated tools (Gélinas et al., 2019b). More research on the validity of behavioural pain assessment tools in specific subgroups is needed to broaden their applicability in critical care. The systematic review and meta-analysis on the diagnostic accuracy of the CPOT revealed that it is an adequate tool but not excellent, requiring further validation in specific subgroups (Zhai et al., 2020). The validity especially of BPS and CPOT have been questioned for brain injured critically ill patients and a new observational tool is under development (Gélinas et al., 2019a). Furthermore, the pain behaviour of patient that are under heavy sedation and neuromuscular blocking is difficult to assess with the current observational pain assessment tools (Gélinas et al., 2019b).

Table 1. The domains and scoring of the observational pain assessment tools developed for critically ill patients.

INSTRUMENT	DOMAINS	SCORING
Behavior Assessment Tool (BOT) (Puntillo et al., 2004)	A List of 38 items including facial responses, verbal responses, and body movement	Each domain: present/absent Total scoring: 0−38
Behavioral Pain Assessment Tool (BPAT) (Devlin et al., 2018)	Facial expressions: neutral, grimace, wince, eyes closed Verbal responses: moaning, complains of pain Body muscle responses: rigid, clenched fists	Each domain: present/absent
Behavioral Pain Scale (BPS) (Payen et al. 2001) **Behavioral Pain Scale Non-intubated (BPS-NI)** (Chanques et al., 2009)	Facial expression, upper limb movements, compliance with ventilation (BPS)/vocalisation (BPS-NI)	Each domain: 1–4 Total Scoring: 3–12
Critical-care Pain Observational Tool (CPOT) (Gélinas et al., 2006)	Facial expression, body movements, muscle tension, compliance with the ventilation/vocalisation	Each domain: 0–2 Total scoring: 0–8
Pain Sssessment and Intervention Notation Tool (P.A.I.N.) (Puntillo et al., 1997)	Behavioral domains: movements, facial expression, posture, vocal sounds Physiological indicators: heart rate, blood pressure, respiration, pallor	Each domain: present/absent
Nonverbal Pain Assessment Tool (NPAT) (Klein et al., 2010)	Emotion, movement, facial glues, verbal glues, positioning/guarding	Each domain: 0−2 or 0-3 (verbal glues: yes/no) Total scoring: 0−10
Nonverbal Pain Scale Initial (NVPS-I) (Odhner et al., 2003) **Nonverbal Pain Scale Revised (NVPS-R)** (Kabes et al., 2009)	Behavioral domains: face, activity/movement, guarding Physiological signs: vital signs, skin (NVPS-I) Respiratory: respiratory rate, oxygen saturation, compliance with ventilator (NVPS-R)	Each domain: 0−2 Total scoring: 0−10

2.2.2 Physiologic parameters in pain assessment

The ability to continuously monitor the patients' physiological status is one of the key factors differentiating ICU from other hospital ward environments. Patient data is continuously displayed and readily accessible for the health care personnel. (Marshall et al., 2017.) Nurses commonly use vital signs for pain assessment (Rose

et al., 2011). Blood pressure, temperature, heart rate, and respiratory rate are usually referred to as vital signs (Lockwood et al., 2004). According to the PADIS guidelines, vital signs are not a valid pain indicator in critically ill patients (Devlin et al., 2018). However, the changes in the hemodynamic status may be pain related, and therefore pain should be assessed with a valid pain assessment tool in cases with fluctuations in the vital signs (Erden et al., 2018).

Physiological changes connected to acute pain in critically ill patients have been widely studied. In most study designs, the physiological parameters are collected at three timepoints: in rest prior to procedures, during and after the care procedures that are known to be painful. Moreover, designs with two timepoints exist; prior to and immediately after the care procedures. The designs often include a nociceptive procedure and a non-nociceptive procedure for a comparison. Turning and endotracheal suctioning are most commonly used as nociceptive stimulus and a non-invasive blood pressure cuff infiltration as the non-nociceptive procedure. (Table 2.)

Table 2. Physiologic measures used for pain assessment in critically ill patients.

MODALITY	MEASURES	MEASUREMENT PRINCIPLE	REFERENCES
Hemodynamic score connected to vital signs	Heart rate	Beats per minute	Young et al., 2006; Gélinas & Johnston, 2007; Siffleet et al., 2007; Li et al., 2009; Arbour & Gélinas, 2010; Kapoustina et al., 2014; Ayasrah, 2016; Hasanin et al., 2017; Cheng et al., 2018; Khanna et al., 2018; Shan et al., 2018; Erden et al., 2018
	Respiratory rate	Respiration number per minute	Gélinas & Johnston, 2007; Arbour & Gélinas, 2010; Kapoustina et al., 2014; Cheng et al., 2018; Erden et al., 2018
	Blood pressure	Systolic: maximum blood pressure during ventricular contraction Diastolic:minimum pressure between the contractions Mean arterial pressure: average pressure during one contraction	Young et al., 2006; Gélinas & Johnston, 2007; Siffleet et al., 2007; Li et al., 2009; Arbour & Gélinas, 2010; Ayasrah, 2016; Hasanin et al., 2017; Cheng et al., 2018; Khanna et al., 2018; Shan et al., 2018; Erden et al., 2018
	Arterial oxygen saturation	The percentage of hemoglobin molecules saturated with oxygen in arterial blood	Gélinas & Johnston, 2007; Arbour & Gélinas. 2010; Kapoustina et al., 2014; Cheng et al., 2018; Erden et al., 2018
Single parameter score	Pupillary reflex dilation	Absolute/changes in pupillar width	Paulus et al., 2013; Fratino et al., 2021; Fratino et al., 2023
	Skin conductance SCA index	Number of fluctuations in skin conductance per second	Khanna et al., 2018; Fratino et al., 2021; Fratino et al., 2023
	Analgesia Nociception Index (ANI)	Computed from high frequency component of heart rate variability	Fratino et al., 2023
Multiparameter score	Nociception Level Index (NOL)	Skin galvanic response, plethysmographic pulse wave, temperature, and accelerometry	Shahiri et al., 2020
	Bispectral Index (BIS)	Electromyographic activity, electroencephalographic data, and the density spectral array	Faritous et al., 2016

The connection of heart rate to procedural pain has been studied in several studies (Abdelhakeem et al., 2021; Cheng et al., 2018; Erden et al., 2018; Khanna et al., 2018; Shan et al., 2018; Hasanin et al., 2017; Ayasrah, 2016; Kapoustina & Echegaray-Benites, 2014; Arbour & Gélinas, 2010; Li et al., 2009; Gélinas & Johnston, 2007; Siffleet et al., 2007; Young et al., 2006). According to most of the studies, heart rate increases during or immediately after a nociceptive procedure. However, the increase might not be statistically significant as shown in study by Siffleet et al. (2007) or heart rate may stay unchanged as in the study of Abdelhakeem et al. (2021). Similar to the heart rate, the respiratory rate usually increases during a nociceptive procedure (Cheng et al., 2018; Kapoustina & Echegaray-Benites, 2014; Arbour & Gélinas, 2010; Gélinas & Johnston, 2007) but might also stay unchanged (Erden et al., 2018). Blood pressure has been measured using invasive systolic blood pressure (SBP), diastolic blood pressure (DBP) and the mean arterial pressure (MAP). The results on blood pressure are contradictory: The increase of SBR and DBR during nociceptive procedure have been statistically significant (Khanna et al., 2018; Ayasrah, 2016) and insignificant (Siffleet et al., 2007), and similar to the heart rate and respiratory rate, they have reminded unchanged (Kapoustina & Echegaray-Benites, 2014). While using the MAP, blood pressure has increased according to the studies (Cheng et al., 2018; Erden et al., 2018; Kapoustina & Echegaray-Benites, 2014; Arbour & Gélinas, 2010; Gélinas & Johnston, 2007). SpO2 tends to decrease during nociception, but it is the weakest of the parameters to respond to nociceptive procedures (Cheng et al., 2018; Erden et al., 2018; Kapoustina & Echegaray-Benites, 2014; Arbour & Gélinas, 2010; Gélinas & Johnston, 2007).

Several studies have used physiological variables to assess pain with other validated pain assessment tools as a reference according to patients' level of consciousness. The number of pain assessment tools used as references is considerable. In the studies, for patients unable to communicate, the CPOT, BPS, BPS-NI and Behavioral checklist measures were used. For patients who were able to communicate, the Numeric rating scale (NRS), Verbal Descriptor Scale (VDS), Faces Pain Thermometer (FPT), Visual Numeric Scale (VNS), Visual Analogue Scale (VAS), and yes/no questions were used. Furthermore, the results regarding the association between physiological measures and the refence measures are contradictory. While some studies found a positive correlation coefficient between pain intensity, heart rate, and respiratory rate levels (Erden et al., 2018; Kapoustina & Echegaray-Benites, 2014; Arbour & Gélinas, 2010), other studies, such as those by Cheng et al. (2018) and Gélinas and Johnston (2007), reported no association between pain intensity and physiological measures.

Conflicting findings from previous studies suggest that changes in haemodynamic parameters and respiratory rate are not specific to pain; they can be affected by several factors such as the conscious status of the patients, medications

and diseases. This led to the exploration of other, potentially more specific physiological pain indicators in critically ill patients. Pupillometry, skin conductance, Analgesia Nociception Index (ANI) have been described as potential pain assessment methods in critically ill patients in ICU. Skin conductance has been studied using the skin conductance algesimeter (SCA) index. The method has found promising; the study by Khanna et al. (2018) found that the SCA Index was more sensitive and specifically linked to pain than other monitored physiological parameters, and was found not to be influenced by circulatory changes and therefore not affected by many drugs. However, there were challenges in measuring the SCA index in a study population including brain injured patients as it was only detectable in 29% of the patients (Fratino et al., 2021).

The use of pupillary reflex dilation has shown some promising findings in pain assessment of ICU patients, and has been used to predict the sufficiency of analgesia before a noxious procedure in patients in ICUs (Lukaszewicz et al., 2015; Paulus et al., 2013). A tetanic stimulus in three levels and a video-based pupillary dilatation evaluation was used to predict the level of analgesia in 34 patients. They found that it was possible to predict an insufficiency of analgesia before endotracheal suction. (Paulus et al., 2013.) Similarly, Lukaszewicz et al. (2015) tested a pupillometric method to assess the adequacy of anaesthesia in intensive care patients before an invasive drainage exchange by measuring pupillary light reflex. The results were promising for the adjustment analgesia before painful procedures. Moreover, approaches which combine these methods with Analgesia Nociception Index (ANI) have been used to assess nociception in critically ill mechanical ventilated patients. The ANI is a measure based on heart rate variability from ECG monitoring. It is a number between 0−100 estimating the balance between parasympathetic and sympathetic outflows. (Fratino et al., 2023.) The study by Fratino et al. (2023) found no correlations between the methods when automated pupillometry, the number of skin conductance fluctuations per second, and the ANI were collected during a tetanic stimulus as a measure of nociception. Furthermore, in an earlier study, the pupillary reflex dilation and SCA showed poor agreement in the assessment of the response to noxious stimulation (Fratino et al., 2021).

In addition to the ANI, two other methods originally developed to monitor nociception during anaesthesia have been studied in patients in ICUs. The Bispectral index (BIS) is a technique measuring nociception from cortical activity and the activity of the corrugator supercilii during anaesthesia. Several studies have found an increase in the BIS during nociceptive procedures in critically ill mechanically ventilated patients (Coleman et al., 2015). However, the BIS index was not primarily developed to assess pain and demands further validation. A novel method, the Nociception Level Index (NOL), was tested for feasibility in 15 critically ill patients for pain assessment. In the study, NOL scores were able to distinguish between

nociceptive and non-nociceptive interventions and were associated with CPOT scores and self-reported pain intensity. (Shahiri et al., 2020.)

2.2.3 Facial expression of pain

The potentiality of facial expressions, among other nonverbal measures of pain, has been the focus of comprehensive research. Facial expressions in humans have both a voluntary and an involuntary aspect. The voluntary aspect has a major role in communicating pain and suffering to others while the involuntary actions are more reflections of autonomic nervous system to nociception (Hadjistavropoulos & Craig, 2002). The studies also describe the most common features of facial expressions that form the "core facial pain expression" (Prkachin & Solomon, 2008; Prkachin, 1992). This include lowering of brows, wrinkling of nose, tightening of orbit, and closing of eyes. In some studies, mouth stretching and opening is described as a part of the core pain expressions (Kunz & Lautenbacher, 2014, 2015; Craig & Patrick, 1985). The universal facial expression of pain has identifiable features. However, the expression's prevalence in individuals differs. The study by Kunz and Lautenbacher (2014) classified the subjects into four phenotypes, each with a different weighting of the features of the facial expression of pain. Furthermore, a group of subjects did not exhibit any activation of the expression.

One of the main frameworks in behavioural science to investigate the face is the Facial Action Coding System (FACS). The framework is used to identify and objectively measure the facial expressions (Ekman & Friesen, 1978). The FACS is usually coded from a video and the code provides precise specification of the dynamics of facial movement in addition to the specific facial actions. The framework divides facial movements into Action Units (AUs) representing individual components of muscle movements producing the expression. There are 46 AUs that have been defined. The reliability of the FACS has been tested and found to be good or excellent (Sayette et al., 2001). However, the use of the FACS requires training and scoring is based on the subjectivity of the scorer (Prkachin, 2009). Several AUs have been identified as being associated with the facial expression of pain but their combination varies between studies (Prkachin, 2009; Prkachin, 1992). (Table 3.)

Table 3. The facial Action Units (AUs) and corresponding muscle basis associated with expression of pain. (Adapted from Paper III)

DESCRIPTOR	FACIAL ACTION UNIT	MUSCLE BASIS	ANATOMICAL CHANGES
Brow lowering	AU41	Corrugator supercilii Depressor glabellae Depressor supercilia	Lowering down of eyebrows Moving eyebrows medially
Cheek raising	AU62	Orbicularis oculi (pars orbitalis)	Appearing of vertical or oblique wrinkles between eyebrows
Lid tightening	AU7	Orbicularis oculi (pars palpebralis)	Pulling of skin toward the eyes Lifting of the cheeks and infraorbital triangle Narrowing the eyes Wrinkling the skin below the eye
Nose wrinkling	AU9	Levator labii superioris alaeque nasi	Tightening and narrowing of the eyelids
Upper lip raising	AU10	Levator labii superioris	Deepening or wrinkling of infraorbital and nasolabial furrow Widening and raising of the nostril wings
Lip corner pulling	AU12	Zygomaticus major	Drooping or oblique movement of lateral corners of the lips
Llp stretching	AU20	Risorius	Bilateral lips stretch

AU= facial Action Unit

The study by Arif-Rahu et al. (2013) is the only study that has determined the specific features of the facial expression of pain in critically ill patients who are unable to communicate using the FACS. According to their results, the strongest activation found was in the upper part of the face and the actions were similar to the identified features in the core pain expression. In addition to lowering of the eyebrows, tightening of the orbit, wrinkling of the nose and closing of the eyes, they found that during nociceptive procedure there was frequent internal elevation of the eyebrows, opening of the mouth, and turning of the head to the right. In the observational pain assessment tools developed for critically ill patients, the facial expression descriptors are used interchangeably. (Table 4.) In all the instruments, the clearest/strongest facial expression connected to pain is described as a grimace. A

grimace is perceived as a clearly visible expression across the face, associated with pain and also other strong negative emotions (Prkachin, 1992). Strong pain-related facial expressions are also described by the terms frown and wince, which may be associated with partial or milder activation of the face. Grimacing, frowning, and wincing are used to identify a certain expression (e.g. in the BOT, BPAT, and P.A.I.N.) or to assess the intensity of the expression (e.g. in the NPAT and NVPS). In the BPS and CPOT, the assessment of facial expression is described in more details using the terminology of the FACS framework. The most descriptors in the assessment tools are located in the upper part of the face which is practical since the lower part is often distorted by the presence of an endotracheal or nasogastric tube (Arif-Rahu & Grap, 2010).

Table 4. The items for assessing the facial expression in the observational pain assessment tool developed for critically ill patients.

INSTRUMENT	ITEMS ON FACIAL EXPRESSION
Behavior Assessment Tool (BOT) (Puntillo et al., 2004)	Grimace/Frown/Wince Eyes closed Grin/Smile Eyes wide open with raised eyebrows Looking away in opposite direction of the pain Mouth wide open /Clenched teeth
Behavioral Pain Assessment Tool (BPAT) (Devlin et al., 2018)	Neutral Grimace Wince Eyes closed
Behavioral Pain Scale (BPS) (Payen et al., 2001)	Relaxed Partly tightened (eg. brow lowering) Fully tightened (eg. eyelid closing) Grimacing
Critical-care Pain Observational Tool (CPOT) (Gélinas et al., 2006)	No muscular tension observed: relaxed Neutral Presence of frown brow lowering, orbit tightening, and levator contraction: tense All of the above facial movements plus eyelid tightly closed: grimacing
Pain Assessment and Intervention Notation (P.A.I.N-) (Puntillo et al., 1997)	Grimacing Frowning Wincing Drawn around month and eyes Teary/Crying Wrinkled forehead
Nonverbal Pain Assessment Tool (NPAT) (Klein et al., 2010)	Relaxed, calm expression Drawn around month and eyes/Tense Frowning/Wincing/Grimacing
Nonverbal Pain Scale (NVPS) (Odhner et al., 2003)	No particular expression or smile Occasional grimace, tearing, frowning, wrinkled forehead Frequent grimace, tearing, frowning, wrinkled forehead

2.3 Automated pain detection

Automated pain detection based on experimental pain databases

Automated pain detection refers to the use of technology, such as sensors and machine learning algorithms, to detect and analyse physiological and behavioural signals to infer the presence and intensity of pain without the use of patient self-

reporting or pain-related behaviour observation. These models can be used to identify patterns within data without human intervention. These patterns can be used to predict and classify future data, to reveal sub-groups of data, or to extract relevant data to find new insights. (Lötsch and Ultsch, 2018.) The research on automated pain detection methods are mainly done on experimental pain databases. One of the most versatile databases is the BioVid Heat Pain Database, including both physiological and video data of ninety study subjects under heat pain induction. The heat pain was induced at four pain levels according to the determined individual pain threshold and pain tolerance. The collected variables include the skin conductance level, the electrocardiogram, the electromyogram of three pain related muscles, and the electroencephalogram. (Werner et al., 2013.) The data has been used in several studies to predict pain using the video based facial action unit (AU) recognition (Werner et al. 2016, 2018). It has also been used to build prediction models to predict pain from physiological parameters (Werner et al., 2014) from the combination of the physiological and facial expression parameters (Gruss et al., 2015). The EMG data from the BioVid Heat Pain database are used less frequently in studies. Limbrecht-Ecklundt et al. (2016) have used both the visual FACS based and EMG methods in the BioVid database to assess their validity for pain intensity prediction. They found that the FACS allowed a reliable distinction between pain threshold and pain tolerance. Correlations between both methods and pain intensity were high, but the EMG and pain intensity increase had a closer relation. Kelati et al. (2022) analysed the EMG data set of the BioVid database. They used data from two facial muscles, the zygomaticus and corrugator supercilii, and succeed in developing a model to predict pain classification with a 99.4% accuracy with binary pain intensity level no pain−high pain.

Automated pain detection in clinical setting

Clinical data have only been used in a few studies to develop pain prediction models using machine leaning in adult patients. Aqajari et al. (2021) formed a research group that built models for automated pain intensity prediction using clinical data collected from post-operative patients using galvanic skin response (GSR) measurement. They were able to build and test several machine learning models with satisfying results with a baseline and five different pain intensity levels using data from 25 post-operative patients. Kobayashi et al. (2021) developed a semiautomated system using machine learning to predict pain in patients in ICUs using continuous vital signs data and other patient information. The retrospective study had a sample with 11 527 patients. They used continuous heart rate, pulse oximetry, arterial oxygen saturation, and arterial blood pressure that was recorded every minute in the model. In addition, the pain intensity assessed with the CPOT, a sedation score and the information on

age and sex were included to the analysis. Additionally, another group conducted a preliminary study using clinical data of patients from an ICU while developing an autonomous pain expression assessment system (Nerella et al., 2021). They collected and analysed a dataset collected from ten patients, including more than 55 000 images. They explored the dataset first using an open source OpenFace platform to automatically detect pain using facial action units (AUs), however, satisfactory results were only obtained using a deep learning method. Clinical challenges emerged using a video-based methodology: the accuracy of the images was hampered by assisted breathing devices, lighting used in the critical care environment, and the orientation of the patient's face to the camera. However, this was the first step to identify pain related AUs in an ICU setting and led to new ICU-pain database with clinical data. (Nerella et al., 2021.)

2.4 Summary of the literature review

The literature review findings show that unrelieved pain is current and one of the most distressing and unpleasant symptoms present for the majority of critically ill patients. Pain management in critically ill patients requires special attention due to the frequent impairment of their ability to communicate and the daily occurrence of multiple painful episodes associated with the treatment of their critical illness and care activities. Systematic pain assessment in critically ill patients leads to more focused interventions to minimise unnecessary suffering and adverse events.

The interpretation of behaviour associated with pain and the recordings of vital signs are the methods that are most used for pain assessment of critically ill patients who are unable to communicate. While physiological parameters are associated with painful events, individual vital signs should not be relied upon pain assessment, as they are not exclusive to pain. Facial expression of pain is one of most prominent pain behaviour but the interpretation of these subtle and transient expressions is challenging. Several observational instruments based on behavioural and physiological pain related changes have been developed for critically ill patients, the most valid and reliable being CPOT, BPS and BPS-NI. However, these methods are subjective, depending on the nurses' education and ability to use the tools and to interpret pain.

Current methods for assessing pain in critically ill patients do not allow continuous pain monitoring as they depend on relatively short observation windows. Continuous monitoring would be essential as pain is often intermittent and of varying intensity. Automated pain detection methods are being developed to meet this challenge, but their development for clinical pain is still in the early stages. New physiological methods are being tested for feasibility in critically ill patients. Some preliminary studies have been conducted on the use of nociception monitoring

methods to detect pain in critically ill patients. In particular, multimodal methods using several parameters seem promising. However, these methods are developed for monitoring the level of nociception during anesthesia, not for pain assessment, and their use for this purpose needs to be carefully studied. To date, only one semiautomatic method has been developed for pain detection in critically ill patients combining continues vital signs monitoring and patient information based on the behavioural pain scale and other patient information. Currently, there is no clinically useful and valid method for continues automated pain detection for critically ill patients who are not able to communicate.

3 Aims

The overall aim of the study was to develop the concept of a Smart Pain Assessment tool based on the Internet of Things (IoT) technology for critically ill patients who are not able to communicate their pain verbally or by other means. The study was conducted within the framework of a medical device development process and describes the early-stage development including two phases and four sub-studies.

The sub-aims and research questions were as follows:

Phase I: Initiation

The aim of Sub-study I was to explore and describe the state of art of the IoT in basic nursing care.

1. What innovations are available for basic nursing care using IoT? (Paper I)
2. In what way is IoT technology used in innovations targeted at basic nursing care? (Paper I)

Phase II: Formulation

The aim of Sub-studies II and III was to explore the initial validity of the concept of the Smart Pain Assessment tool for pain detection.

1. What is the validity of the chosen parameters in relation to pain intensity? (Papers II and III)
2. In what way is the system capable of detecting experimental pain in healthy adults using the chosen machine learning algorithms? (Papers II and III)

The aim of Sub-study IV was to evaluate the feasibility of the Smart Pain Assessment Tool concept by the potential future users for and to involve the users in the development process.

1. What are the perceptions of critical care nurses regarding the use of smart technology in pain assessment? (Paper IV)
2. How do critical care nurses evaluate the feasibility of the proposed Smart Pain Assessment tool? (Paper IV)

4 Materials and Methods

4.1 Methodological approach

4.1.1 Medical device development process

Briefly, medical devices are defined according to the Medical Devices Regulation (EU) 2017/745 (MDR) as "any apparatus, software, material or other similar or related article, intended to be used for specific medical purposes: diagnosis, prevention, monitoring, treatment or alleviation of a disease or an injury". The development of medical devices is regulated by the European Union (EU) in Europe and by the U.S. Food and Drug Administration (FDA) in the United States. The purpose of the regulation is to provide effective and safe devices for users. The regulation is also aimed at improving the availability of innovations on the market. In the EU, the regulation of medical devices has been reformed over the last few years and the Regulation (EU) 2017/745 on medical devices (MDR) was applied in May 2021. (Fimea, 2021.)

The medical device development process describes the development and regulation of a medical device step by step. Typically, the medical device development process is described through five stages, but the concepts and details of their content vary. The FDA process description includes four steps: 1) device discovery and concept, 2) preclinical research-prototype, 3) FDA device review, 4) FDA post-market device Safety monitoring (FDA, 2018). The development process is not described in the EU through the same type of phases, but focuses on the regulations at different stages, in particular through the ISO standards. In this study, the phases described by Pietzsch et al. (2009) for medical device process is used. (Figure 1.) This model was developed by reviewing the literature on medical device development processes. The model identifies five phases from initiation to product launch. Phase I includes early evaluation of the clinical needs and reviews on the technological concepts and existing technology. Phase II includes an iterative concept and prototype analysis with continuous interaction among developers and future device users. Phase III concentrates on feasibility studies, verification testing, and user prototype evaluations. These continue before the final formal validation

performed in Phase IV. In Phase V, the product is launched and postmarketing surveillance assessment is conducted. (Pietzsch et al., 2009.)

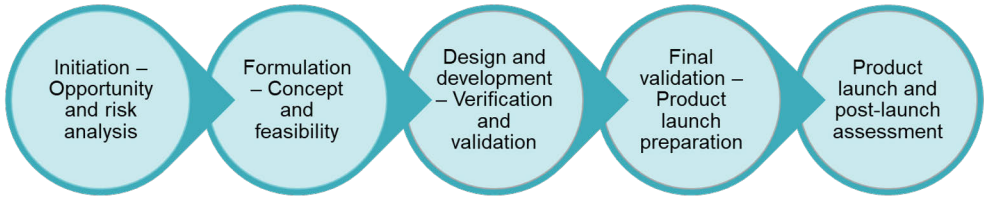

Figure 1. The medical device phases of the development process (Pietzsch et al., 2009).

The development process reviews and the approval for marketing of a medical device are done by named notified bodies, accredited by Member State Health Ministries. In Finland, the Finnish Medicines Agency Fimea is responsible for the administration of medical devices. Fimea controls the safety of medical devices and their operability before they become available on the market. The medical devices that conform with existing regulations are marked with the CE conformity markings. (Fimea, 2021). Before starting the clinical study, the Smart Pain Assessment tool research was registered with the National Supervisory Authority for Welfare and Health (Valvira), which is the authority controlling the medical devices prior to Fimea. The medical devices are divided to four classes that are associated with the intended use of the device. The classes are divided according to the risk the device poses to the patient, and the intended use, invasiveness, and local vs. systemic effects are also assessed. (Regulation (EU) 2017/745.)

4.1.2 The Internet of Things

The proposed device under development in the study uses the Internet of Things (IoT) technology, a system enabling “things” or objects to be connected to the Internet (Atzori et al., 2010). The IoT is a network of connected objects or things, characterised by autonomous regulation, administration, and control. In practice, the IoT connects devices, other objects and systems with sensors or Radio Frequency Identification (RFID) and Wireless Local Area Network (WLAN) chips, allowing these devices to be controlled and interact. The technology enables continuous and simultaneous collection, analysis and display of heterogenous data.

The architecture of the IoT-based system in consist of four layers according to the structure and functions of the system; these layers include sensing, networking, services, and application (Xu et al., 2014). The sensing layer is the sensor network which collects the heterogeneous data from devices, sensors and actuators. This is

the layer closest to the clinical environment. The networking layer acts as a bridging component via wireless protocols such as Bluetooth and Wi-Fi between the sensor network and the service layer. In the networking layer, a gateway transfers and pre-organizes the collected data for further usage to a remote or local server in the cloud. The data is transferred via gateway to the service layer for processing and service creation. The cloud generates information from heterogeneous the data through data analytics and semantic processes. The data processed in the application layer is displayed to the end user in a usable format through user interfaces. (Xu et al., 2014.) A smart gateway can also improve system performance by reducing latency and managing outages when Internet access is not available (Rahmani et al., 2015).

4.2 The Smart Pain Assessment tool innovation

The Smart Pain Assessment tool is an innovation targeted to detect acute pain in patients unable to communicate in ICU environment. The proposed Smart Pain Assessment tool is an IoT-based, smart, wireless system that collects data simultaneously from selected physiological parameters. The parameters include the heart rate (HR), respiratory rate (RR), galvanic skin response (GRS), and facial muscle activity using surface electromyography (EMG). Data collected from multiple sources is transferred wirelessly to a smart gateway and on to a cloud service for data storage and analysis. (Figure 2.) The system is able to detect the pain automatically using advanced data analytics and machine learning. The pain intensity is displayed to healthcare personnel via automated notifications in the patient monitor.

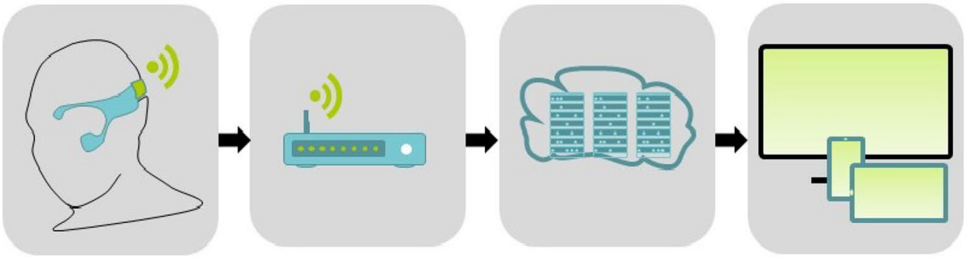

Figure 2. The Smart Pain Assessment tool based on IoT technology. (Adapted from paper IV)

The system is structured in four layers according to the architecture of the IoT technology:

1. The sensing layer: The method includes wearable, wireless sensors that do not interfere with patient movement and remain in place even when the patient is restless. In addition to other wearable sensors, the method

includes a sensor mask that is attached to the patient's face to measure facial muscle activation. The sensor mask covers the facial muscles that are connected to pain expression (Yang et al., 2018).

2. The networking layer: The system transfers the data via wireless WiFi to the gateway.
3. The service layer: In the cloud service and with a special Fog computing service, the data can be combined and classified into different degrees of pain through machine learning and data analytics.
4. The application layer: The pain related data is displayed to the end-user through the user interface.

4.3 Study design

The study was conducted in two phases and four sub-studies following the early phases of the medical device development process (Pietzsch et al., 2009). (Figure 3.)

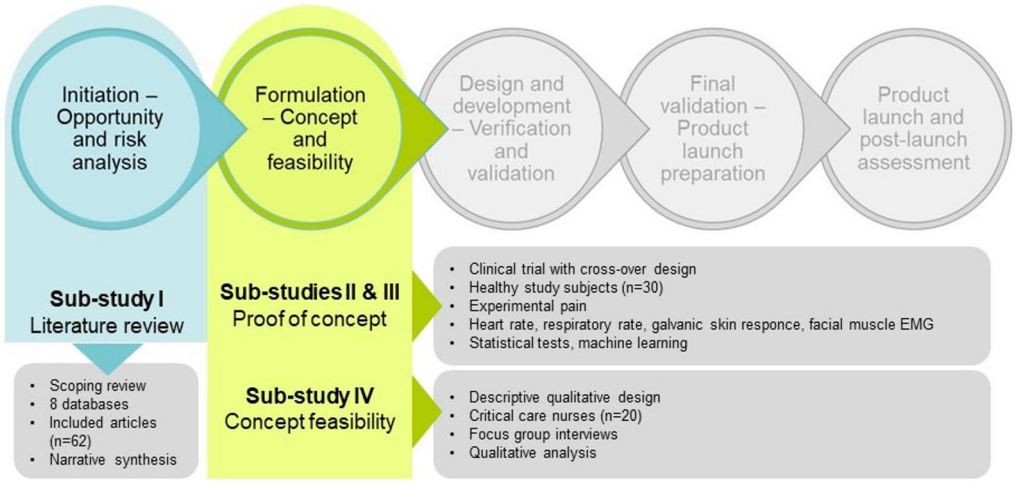

Figure 3. The study design as part of the medical device development process.

The initiation Phase I included a scoping review, which aimed to explore the novel technology paradigm in nursing care. The formulation Phase II included Sub-studies II-IV and aimed to develop and test the feasibility of the concept. In Sub-studies II and III, data from a clinical trial with a cross-over design and experimental pain induction were used. In Sub-study IV, the feasibility of the concept of the Smart Pain Assessment tool was evaluated by critical care nurses as potential future users of the device. The study was conducted as a descriptive qualitative study with focus group

interviews. The methodology of each phase and sub-study are presented as a summary in Table 5. Sub-studies I-IV and corresponding publications (referred as Papers I-IV) are numbered accordingly.

Table 5. Summary of the methodological approaches of the study.

PHASE	SUB-STUDY	DESIGN	SETTING	SAMPLING AND SAMPLE	DATA ANALYSIS	REPORTED IN
INITIATION PHASE I	I	Scoping literature review	Databases: ACM DL CINAHL Google Scholar IEEE Xplore DL PubMed ScienceDirect Scopus SpringerLink	The literature on IoT innovation targeted to basic nursing care in hospital eligible literature, sample (n=62)	Narrative synthesis	Paper I
FORMULATION PHASE II	II & III	Prospective, observational study with cross-over design	Laboratory, university campus	Purposive sampling, healthy volunteers (n=31)	Statistical tests, supervised machine learning	Papers II and III
	IV	Qualitative descriptive study	Level III intensive care unit	Purposive sampling, critical care nurses (n=20)	Inductive and deductive content analysis	Paper IV

4.4 Materials and methods used in the initiation Phase I (Paper I)

4.4.1 Sample, setting and data collection

A scoping review method was used to identify and map the state of art of the IoT technology used in basic nursing care according to the current research literature. Scoping review is suitable for emerging research areas because there might be diversity in the methodologies and there is a need to identify the main sources and types of evidence available (Arksey & O'malley, 2005; Colquhoun et al., 2014). The scoping review framework (Arksey & O'malley, 2005) guided the review in five stages1) identifying the research question 2) identifying relevant studies 3) defining

the selection of relevant studies 4) extracting the data, and 5) compiling, summarising and reporting the results.

The literature search was done using eight databases and employing search terms to suit the topic in different research fields (See Paper I, Table 1.). The search was conducted in two parts: In the primary search, the databases Pubmed, CINAHL and Scopus (nursing subject area) were searched using a Boolean combination of the terms "Internet of Thing" OR "IoT" to find the nursing care related literature on IoT technology. In the five technological databases, the terms "Internet of Things" AND "Nursing" OR "Hospital" were used. A further search of these databases was carried out, replacing the term Internet of Things with selected basic nursing terms to find literature with more detailed information. The search was conducted in March and April 2016. An additional search in Pubmed, CINAHL and Scopus also included the term "nursing informatics". The English language was used as a limitation. No time limit was used in the primary search, but the search concerning nursing informatics was limited to the years 2006 to 2016. The literature published in scientific publications concerning basic nursing care in hospital environment was included. IoT based solution for health-related self-monitoring or remote monitoring were excluded as well as papers only describing technical development. The study selection was done and reported according to PRISMA guidelines.

4.4.2 Data extraction and analysis

The characteristics of the eligible studies were extracted, and the type of the article and study design were analysed. In addition, if mentioned, the main target patient group was specified into age groups. The Internet of Things based innovations were identified and classified into basic nursing care topics. For this, a narrative synthesis and deductive approach were used as the innovations were categorised according to the definition of basic nursing care for hospitalised adult patients (Englebright et al., 2014); these were based on Henderson's (1964) description of the 14 fundamental needs of the patients. By definition, these activities are common to all adult hospital patients, without reference to a specific health problem or patient outcome (Englebright et al., 2014).

4.5 Materials and methods used in the formulation Phase II (Papers II−IV)

4.5.1 The study designs, participants and settings

Sub-studies II and III were conducted as a clinical trial with a cross over design. Experimental pain was used to collect data in order to validate the initial prototype

of the Smart Pain Assessment tool. The study population consisted of working-age (18−65 years old) healthy adults. Participants who had healthy skin in the facial area and upper extremities and were able to communicate in the Finnish language were included. The exclusion criteria included any acute and chronic illnesses, medication use during the study or the previous two weeks, pregnancy, and Body Mass Index < 30. In addition, excessive facial hair in the sensor site was a reason for exclusion. The participants were recruited via advertisements on notice boards on the university campus and through the university webpage. The data was collected between December 2015 and March 2016.

The data was collected in a technical laboratory in the university campus area. A technician and a study nurse were present at the data collections. The aim was to obtain a purposive sample of 30 participants with an even distribution of male and female study participants. The final data consisted of 31 participants data because of technical challenges in some of the collection sessions.

In Sub-study IV, the participants were the professional end-users of the medical device under development. A focus group design was used to involve the critical care nurses working in the ICU to the Smart Pain Assessment tool development process. The participants were recruited using a purposive sampling method (Andrade, 2021). Participants who had minimum of a one year of working experience in an ICU, experience of working with noncommunicative patients, and were willing to participate in the focus group interviews were included in the study. All participants (n=20) were registered nurses. The interviews took place in a level III ICU of a university hospital in April and May 2019. The recruitment was done via a contact person in the ward administration, who contacted the critical care nurses and organised the groups according to their work shifts. The focus group interviews were conducted during the morning shifts in the ICU meeting room.

4.5.2 Data collection instruments and procedures

In Sub-studies II and III, the data was collected using several instruments during experimental pain induction. **In Sub-study IV**, the data was collected using thematic interviews in focus groups.

Instruments for measurement (Papers II and III)

Bioharness. A wearable Bioharness 3.0. device was used for detecting the heart rate and respiratory rate of the study subjects. Bioharness 3.0 (Zephyr Technology, Annapolis, Maryland, US.) is a device for monitoring physiological parameters of adults in non-medical use. The device consists of a chest strap and an electronics module for signal detection attached to the strap. The device collects data from

electrocardiography (ECG), heart rate (HR), and respiration rate (RR); body orientation and activity can also be detected. The pressure sensors for detection of the breathing movement of the rib cage is located in the elastic strap, as well as the passive sensors for the ECG detection. The data is collected and transmitted with the Bioharness module attached to the chest strap. The Bioharness 3.0 is wireless and operates with an internal rechargeable lithium polymer cell. The collected data is sent wirelessly via Bluetooth or 802.15.4 frequencies.

Facial surface electromyography (EMG). A multi-functional biosignal acquisition device, developed by the research group, was used to collect the EMG signal. The device has the capacity to acquire signals from eight channels, with a 24-bit analogue-to-digital resolution. The signal was sampled at a rate of 1000 samples per second. (Jiang et al. 2016.) The configuration was chosen to be monopolar because of the relatively small size of the facial muscles and the future aim to develop a clinically usable wearable sensor mask for the EMG measurement. The sensors were applied on the right side of the face. Five facial muscles were selected to measure expression during the experimental pain induction: corrugator supercilii, orbicularis oculi, levator labii superioris, zygomaticus major, and risorius. The muscles were chosen based on knowledge of corresponding Action Units and muscle basis. (Table 3.) The reference electrodes were set on the bony area behind the ear and on the frontalis muscle.

Galvanic skin response (GSR). The skin conductivity using galvanic skin response was used to measure the sympathetic arousal during pain induction. The GSR measured the changes in sweat gland activity and it was captured by detecting the changes in electrical conductivity using Ag/AgCl electrodes. The electrodes were attached to the middle and index fingers. The device was made by the research group.

Self-reported pain assessment tool. The self-reported pain was assessed in order to label to collected data with pain intensity labels. A visual horizontal, 11-point (0−10) NRS-measurement was used in the study (Breivik et al., 2008). The use was introduced to the participants before the start of the data collection. The point of NRS 3 was emphasised as a threshold for meaningful pain. The participants were asked to report the experienced pain intensity on the NRS scale at the end of the pain exposure but these reports were not used in the analysis in the current study.

Instruments for experimental pain inducement (Papers II and III)

Transcutaneous electrical nerve stimulation (TENS). The transcutaneous electrical nerve stimulation device (TENS, Sanitas, Hans Dinlage GmbH, Germany) was used to induce a painful electrical stimulus. A pre-installed program with pulse

width of 250 μs and the frequency of 100 Hz was chosen after pretesting the device. The TENS output was manually increased by the study nurse every three seconds from level 0 to a level, until the participant reported intolerable sensation or reached the maximum level of 50 (peak to peak voltage 2V per level at 500 Ohm). The electrical stimulus was induced on the fingertip of the forth finger.

Heating element. The heating element used in the study was developed by the research group. The heating element had a round metal contact surface with 3 cm diameter. The temperature rose by 1°C every three seconds until it reached 45°C, and then continued to increase by 1°C every five seconds until it reached a temperature of 52°C. The heat pain was induced on the inner arm of the participant. A cold pad was applied to the skin after removing the heating element to cool down the skin and avoid burns.

Procedures (Papers II and III)

The participants sat in an armchair during the data collection. The preliminaries included cleaning of the skin under the electrodes, and attaching electrodes and the Bioharness belt. The stimulus started from a non-painful level and rose constantly as prescribed. The participants were informed to press a signalling button first time when the sensation started to feel painful (NRS 3−4), and again, when the pain felt intolerable, and participant wanted to stop the test. Each participant had four pain tests; two times in each pain inducement method. The order of the pain inducement methods and sites were randomised to avoid the order bias. A baseline period was recorded before testing. The participants were instructed to avoid talking during the pain inducement and measurements. The procedures are described in detail in Papers II and III, and the parameters and data collection methods are presented in Table 6.

Table 6. The parameters and methods used in data collection in sub-studies II and III.

PARAMETER	METHOD	DATA COLLECTION
Electrical potential of the facial muscles associated with the expression of pain (corrugator supercilii, levator labii superioris, orbicuralis oculi, zygomaticus major and risorius)	Surface electromyography (EMG) Self-developed device	Surface sensors applied with monopolar configuration on the right side of the face (pre-gelled H124SG Ag/AgCl sensors size 30 mm × 24 mm)
Skin conductivity	Galvanic skin response (GSR) Self-developed device	Sensors attached to the middle and index fingers opposite site to the pain exposure
Respiration rate (RR) Heart rate (HR)	Electrocardiography (ECG) Bioharness 3	Sensors attached to the belt worn around the chest by a participant
Self-reported pain threshold and tolerance	Visual horizontal numeric rating scale (NRS)	Collected in two time points: 1) when the stimulus reaches painful sensation (threshold) and 2) when the pain intensity reached intolerable level (pain tolerance)

Focus group interviews (Paper IV)

In Sub-study IV, focus group interviews (n=5) were conducted in May 2019. Two researchers and four participants attended each focus group. One researcher was responsible for conducting of the interviews and the other researcher simultaneously took notes and handled the technical recording. The participants' background information (age and work experience in ICU) was collected with a form at the beginning of the interview. The interviews were structured around three themes 1) the challenges faced by nurses in assessing the pain of patients who are unable to communicate 2) future visions for pain assessment technology, and 3) evaluation of the concept of the Smart Pain Assessment tool. The Smart Pain Assessment tool concept was introduced in the focus groups for an evaluation of the visual illustration and verbal description. The interviews were audio-recorded and transcribed. The interviews lasted from 42 to 54 minutes. The saturation of the data was assessed initially during the data collection process using the notes and the preliminary coding of the data.

4.5.3 Data analysis

Analysis of the bio-signal data (Papers II and III)

The raw data included the physiological HR, RR and GSR data and EMG data from facial muscles. The signal data was first preprossessed and standardised. The pain labels were applied and the parameters and their correlations were statistically tested before classification. The prediction models were verified before the final output as a prediction of pain intensity. The data analysis was done by two members of the research group with expertise in data analytics and machine learning. (Figure 4.)

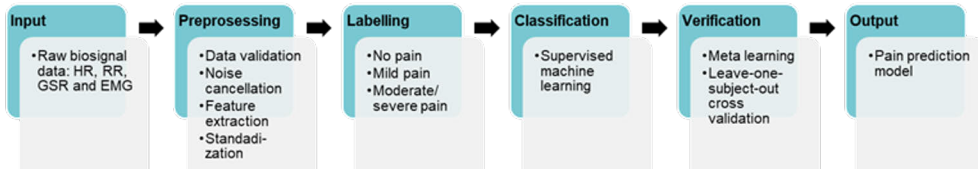

Figure 4. The data analysis process in Sub-studies II and III.

The input was the raw biosignal data collected from multiple data sources during the four pain inductions in each study participants.

Preprossessing and feature extraction. The signal processing was done with the MATLAB programming platform in Sub-studies II and III. The preprossessing included the elimination of noise and verification of validity of the collected data. The noise in the data was caused by movement artefacts, drift in low frequencies at the baseline and electrical pulses of the TENS device. In Sub-study II, after the validation check, the physiological signals were standardized and the 13-dimensional parameter matrix described in details in Paper II. In Sub-study III, the facial muscle signals were standardised, recomposed and downsampled from1000-Hz to1-Hz features leading to ten features with root mean square (RMS) and a wave form length (WL).

Data labelling was done to allow exploration of the collected parameters at different pain intensity levels. In Sub-study II, the labels were the baseline before the start of the pain induction (t0−30sec), “no pain” period after the stimulus start (t0), “mild pain” period until the pain threshold (t1) and “moderate/severe pain” period until the pain tolerance (t2). In Sub-study III the correspondent test periods were labelled using the timepoints of the stimulus start (t1), subject-reported pain threshold (t2), and pain tolerance (t3). Sub-study III aimed for closer exploration of the pain intensity during the test periods and the test periods were divided into four shorter period labels P1–P4. The test period P0 was set to the baseline for the 30-second period preceding the start of pain induction.

Statistical analysis. Before the classification, the parameters were tested statistically to determine the strongest parameters to be used in the models. In Sub-study II, a correlation analysis was done with Pearson's linear correlation coefficients between each standardized parameter and the pain intensity labels. The data analysis in Sub-study III was done using a Python (2.7.14 and 3.6.3) and included a pair-wise comparison with a Wilcoxon signed-rank test.

Classification. An Artificial neural network algorithm (ANN) was used in Sub-study II to classify the pain labels from the input features. The parameters of the matrices were used as the input and the three pain intensity labels as the output. The architecture of the model is presented in details in Paper II, figure 4. The receiver operating characteristic (ROC) curve was used for each classification. The area under the ROC curve (AUC) was evaluated in addition to the average accuracy to present the performance of the classification (Hanley & McNeil, 1982). The true positive rate (TPR) was used for the evaluation of the proportion of correct identification of each pain intensity level. In Sub-study III, a supervised machine learning method k-Nearest Neighbour (kNN) was applied. kNN is a basic supervised machine learning algorithm for classification tasks that identifies the k nearest data points in the training set based on some similarity metric and assigns the new point the most common class (LaRose et al, 2014). The self-reported pain threshold and tolerance were used to detect the pain intensities in the three labels. As a result, the concordance index (c-index) was used to calculate the concordance between the real ordinal outcomes and model predictions. The c-index is a measure to show how well a predictive model can distinguish between individuals who experience an event and those who do not, ranging from 0.5 (random result) to 1.0 (perfect prediction) (Longato et al., 2020).

Evaluation. In Sub-study II, a Leave-one-subject-out cross-validation was done as part of the ANN classifier to see, how the method adapted to a fresh subject. In Sub-study III, nested cross-validation was used to ensure that the performance of the classifier was not the result of random variation, but that there was a real link between the input data and the labels.

The output was a pain prediction at three pain intensity levels (no pain–mild pain–moderate/severe pain).

The qualitative data analysis (Paper IV)

In Sub-study IV, a qualitative data analysis was done using a deductive approach (Kyngäs & Kaakinen, 2020). The deductive analysis was based on the part of Rogers's Diffusion of innovation theory describing the features of feasible innovation (Rogers, 1983). The theory was used to define those attributes of the technology that will influence its adoption by future users. These attributes include:

relative advantage - the extent to which users perceive benefits or improvements from adopting the innovation; *compatibility* - the extent to which the innovation is in line with the values, experiences and needs of the users; *complexity* - the difficulty of understanding and/or using the innovation; *trialability* - the extent to which and how the innovation can be tested or experimented with; *observability* - the extent to which the innovation produces visible and concrete benefits. (Rogers 1983.)

Following the deductive analysis, data that did not fit the theory or did not describe the feasibility from a device perspective were analysed using an inductive approach (Graneheim & Lundman, 2004). The inductive analysis was done to cover such topics that was not covered in the deductive analysis using the Diffusion of Innovation theory as a framework. It was proceeded in an iterative process in which initial expressions were condensed and coded. The codes were classified into subcategories and by abstracting further to the main categories. The codes were reviewed by the other members of the research group and the codes as well as the categories were revised several times to reach their final form.

4.6 Ethical considerations

Research integrity

The research integrity was established by following the guidelines for responsible conduct of research and procedures for handling allegations of misconduct in Finland (TENK, 2023). The clinical studies were subject to ethical review and the relevant research permissions were obtained. For reporting of the studies, we used the relevant guidelines according to the Enhancing the QUAlity and Transparency Of health Research (The EQUATOR Network). When defining the authorship of the publications, we followed the Vancouver recommendations of the authorship by the International Committee of Medical Journal Editors (ICMJE, 2023). The data from the clinical studies was kept confidential in the Seafile, which is a cloud storage maintained by the university on its own server. Only authorised members of the research team had access to the data. The data were pseudonymised and kept separate from the identification data of the participants. Data from the sub-studies will be kept for the period specified in the study plan and destroyed in a secure manner.

Ethical considerations in experimental pain research

In Sub-studies II and III, we induced experimental pain in the participants, which requires the researcher to be particularly careful about the ethics of the study. The ethical considerations were reviewed using the Ethical Guidelines for Pain Research in Humans by the International Association for Study of Pain (International

Association for Study of Pain, 2021). The guidelines were realised in the study as follows:

The study protocol review and approval by an independent and expert human research committee. The protocol of Sub-study II and III was approved by the Ethics Committee of the Hospital District of South West Finland (ETMK:83/1801/2015) and medical device research was reported to the National Supervisory Authority for Welfare and Health in compliance with the relevant procedures at that time. As some of the devices used in the study were not CE marked, a separate report on their use and characteristics was made as an annex to the application for the ethical review.

The participants right to informed consent and information on the objectives and procedures. The participants received both oral and written information on the study and an opportunity to ask questions and to discuss with the researcher before signing a written informed consent. The participants were aware about the aim and methods of the study and possible risks related. They were also aware that there was no direct benefit to the participants. The study was carried out by individuals trained in health care. A safe and confidential research environment was created and each participant was treated as an individual and on an equal basis to support the psychological wellbeing during the study. The participants were aware that they could withdraw their participation at any time. The study was discontinued if the researcher thought it would be in the best interest of the participant. An anaesthesiologist was available for consultation in case of adverse events during the data collection phase. Unexpected effects in the data collection were recorded and the data collection practices reviewed in cases where adverse effects were experienced by the research group.

Vulnerable subjects in pain research. The Smart Pain Assessment tool development study aims to develop a clinically applicable pain assessment method for critically ill patients who are unable to communicate verbally or by other means. Patients who are unable to communicate are considered to be a vulnerable group as their pain might stay unrecognised or can be under- or over-treated (Herr et al., 2019a). The current definition of pain by IASP is followed by six notes, one of which is to clarify that verbal communication is only one form of pain expression and that the possibility of pain should be considered for all living beings (Raja et al., 2020). Experimental pain research balances the ethical principles of beneficence (duty to benefit) and nonmaleficence (duty not to harm). These same ethical principles also guide the overall aim of the study, which is to develop a new pain assessment tool, as they oblige healthcare professionals to provide the same quality of pain care and comfort to all patients, including vulnerable patients who are unable to communicate. (Herr et al., 2019a). In this study, the development of the instrument is at an early

stage and therefore the study used healthy volunteer patients to test the prototype device.

Use of the stimulus in experimental pain research. The research must not in any way harm the subject physically or psychologically or offend their values. As this study requires the participants to be subjected to local and at most moderate pain, it was carried out with particular care and caution. The study followed the principle that participants should be able to interrupt the pain stimulus at any time and the amount and intensity of the painful stimuli should be kept to a minimum (Birnie et al., 2014). This was ensured by carefully pre-testing in advance by the research team of the mechanisms of pain induction, pain intensity regulation and related measurement used in the study. Both stimuli had predefined safety limits that were followed. The sample size of the study was kept as small as possible for ethical reasons, that is so as to provide the necessary research data, but avoid causing unnecessary pain.

Ethical considerations on the focus group study

Sub-study IV was approved by the Ethics Committee of the University of Turku (Statement nr.7/2019) and was subject to a request for research permission from the hospital organisation (TP2/002/19) where it was carried out. The participants received both verbal and written information about the study before signing a written informed consent. The participants were aware that they were free to withdraw from the study at any stage. The focus group interview topic was non-sensitive and focused on the use of technology in nursing and nursing practice in pain management. Participants were recruited through the ward contact person, who disseminated information about the study to the ward nurses. Participation in the study was voluntary and those interested expressed their interest in taking part to the contact person. Before informed consent was obtained, participants were given time to familiarise themselves with the written study information material. They had the opportunity to ask questions about the process and purpose of the study.

The interview was designed so as not to burden the participants more than necessary. The focus groups were conducted during the work shift, as work arrangements allowed, and lasted under 60 minutes. The moderation of the focus group interview focused on ensuring that everyone had an equal opportunity to participate in the discussion, but also considered the possibility for participants to opt out of the discussion if they wished (Sim & Waterfield, 2019). In the final research report, care was taken to ensure that none of the participants could be identified as the quotes were reported at focus group level.

5 Results

In this chapter, the results of the study are presented based on the phases of the medical device development framework and the study aims. First, the results from the initiation Phase I (Paper I) provide a theoretical background of the technology used for basic nursing care. Subsequently, the results from the formulation Phase II present the findings from the testing (Papers II and III) and evaluation (Paper IV) of the Smart Pain Assessment tool concept.

5.1 Possibilities of the Internet of things technology in the initiation Phase I (Paper I)

The results of the scoping review were part of the scientific groundwork done during the initiation Phase of the development work for the Smart Pain Assessment tool. In the scoping review, 62 eligible papers were included; these papers were published between the years 2008−2016 and presented technological development and testing of innovations using IoT targeted to basic nursing care in hospital environment. The majority of the research was published as proceedings of technological conferences. The methodologies in the included studies were diverse: the major of the studies were concerned with testing the usability and feasibility of early designs. There were no trials with comparisons or randomised study designs.

The innovations were classified using activities of the basic nursing care according to a model developed for basic nursing care in electronic health records by Englebright et al. (2014). All together 70 basic nursing care topics were found. These were further classified into four activities in basic nursing care: 1) comprehensive assessment including baseline assessments of patients, 2) periodical clinical reassessment including regular assessments throughout the hospitalisation, 3) activities of daily living consist of the patient's basic physical needs, and 4) care management including coordination of activities in care team (Englebright et al., 2014). (Table 7.) Especially the vital signs were used in various ways; mostly the vital signs were used to monitor the patients' physiological condition, but they were broadly used in innovations targeted to neonatal monitoring, sleep and rest detection, pain detection and activity monitoring. Other areas with several innovations included

falls monitoring and prevention, and hygiene monitoring in the hospital environment.

Only one innovation was found connected to pain assessment. An IoT based pain and discomfort detection system for new-borns collects both physiological and behavioural parameters connected to pain in new-borns: heart rate, respiratory rate, blood oxygen level, blood pressure, body and head movements, frowning, lips movement, eyes open/closed, sleeping periods, and vocalisation. The proposed system includes data collection with sensors, web camera video and audio processing attached to an incubator, a system for processing and analysing the pain and discomfort and a log of the information for health professionals and parents. (Martínez-Ballesté et al., 2014.) However, the paper was a methodological proposal of the system published in a conference proceeding without clinical testing.

Table 7. The topics of IoT enabled innovations in basic nursing care.

BASIC NURSING CARE AREAS	TOPICS	(n)
PERIODICAL CLINICAL REASSESSMENT	Physiological monitoring	13
	Neonatal monitoring	2
	Pain and discomfort	1
	Medication	6
	Sleep and rest detection	6
ACTIVITIES OF DAILY LIVING	Secretion	7
	Fall detection	10
	Activity monitoring	3
	Decision support system	6
CARE MANAGEMENT	Tracking (personnel, patients, devices)	3
	Nurse calling system	3
	Hygiene	9
COMPREHENSIVE ASSESSMENT	Comfort and play	1

The studies were analysed to determine which layers of the IoT technology architecture they described in relation to basic nursing care. The majority of the studies (49/62) described the development of the perception layer, meaning the development of sensors and other data sources, and the validation of data collection methods. In addition, the cloud layer development was described in 44/62 of the studies including the machine learning models used and their validation. The

development and function of the gateway layer was less seldom described. The results of the analysis are presented in details in paper I, Table 2.

The innovations targeted to basic nursing care using IoT used multiple data sources. (Figure 5.) In the majority of the innovations, the data were collected from the patients with non-invasive and wireless sensors. Ambient sensors collected data from the environment, such as pressure sensors in the mattress to detect real-time sleeping patterns and physical activity during the hospitalisation (Liu & Hsu, 2013). Moreover, some of the vital sign monitoring was done by measuring parameters from the environment; for example, the breathing rate and pattern were measured with a paper-based sensor attached to breathing mask from the changes in humidity caused by cycles of inhalation and exhalation (Güder et al., 2016). Another area where the data was collected from the environment was secretion; an intelligent system based on IoT for detection of continence was proposed by Wai et al. (2010), collecting data from diapers with a wetness sensor. Nurses or other health professionals were less frequently used as sources of information. Innovations to improve hand hygiene included the collection of positioning data on caregivers entering and leaving patient rooms and the enforcement of hand disinfection (Baslyman et al., 2015). An example of an innovation that combined location data collected from nurses and patients is the proposal by Kanan and Elhassan (2015) for a new type of nurse call system that sends a call from the patient to the nurse who is available and closest to the patient. Methods that collect data from all three analysed sources (patient, nurse and environment) were the most common innovations in two areas: the intelligent decision support systems and the tracking of patients, staff and equipment. An example of such IoT-based innovation is the intelligent, context-aware decision support system proposed by Manate et al. (2014). This combines location-based and patient physiological and psychological status monitoring into seamless healthcare services in a hospital environment.

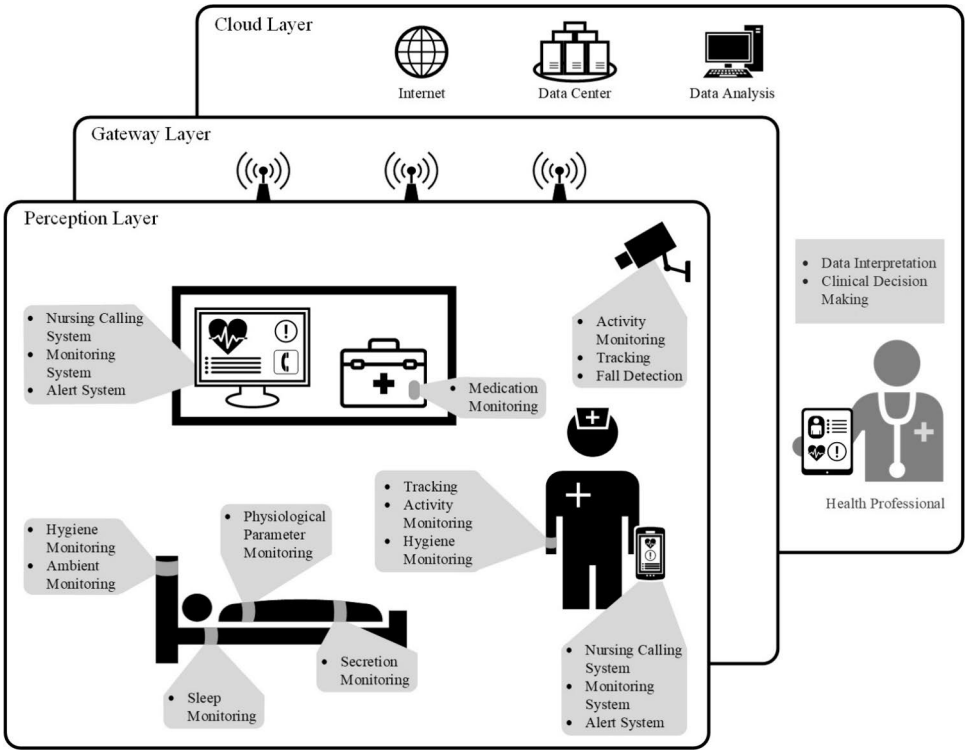

Figure 5. The IoT based innovations in basic nursing care described together with the IoT architecture. (Adapted from Paper I)

5.2 The concept and feasibility of the Smart Pain Assessment tool in the formulation Phase II (Papers II–IV)

The feasibility of the concept of the Smart Pain Assessment tool was first established by testing the prototype of the facial EMG device and by measuring the chosen physiological parameters with commercial and research technology. The collected sample used in Sub-studies II and III consisted of 31 working-aged healthy participants (15 males and 16 females) 21–51years (33 ± 9.0 years). In Sub-study II, the data of 30 participants (15 males and 15 females) were valid for the analysis. In Sub-study III the facial muscle EMG data from the 31 participants was included (15 males and 16 females). As each participant had four tests, the number of the test in the sub-studies were 116 and 120, respectively. The average length of one test was 108 s (SD 39). In these results, all the four tests (two electrical and two heat) were analysed together to be in line with the aim to build a general model for acute pain intensity prediction.

5.2.1 The validity of the parameters for automated pain detection (Papers II and III)

The validity of the parameters selected for pain detection was examined in relation to self-reported pain, which was reported as the pain threshold and tolerance during pain induction. Pain intensity was examined using gradually increasing stimulus intensity and time points t0-t3 (stimulus onset/pain threshold/pain tolerance). In Sub-study II, pain was classified into three categories: no pain (baseline) mild pain (before pain threshold), and moderate/severe pain (before pain tolerance).

In Sub-study II, Pearson's linear correlation coefficients were used for correlation analysis between the parameters and the pain intensity level. The correlation of the parameters was observed over both physiological and facial muscle data, using the two preprocessed matrices, the median matrix and the parameter matrix separately. The best three parameters for prediction were GSR, HR and RR. GSR and HR were correlated positively to the pain intensity level and RR was correlated negatively, meaning the first two increased and the last decreased as the pain intensity increased. In the correlation analysis of the facial muscle parameters, the facial muscles features had lower values than the physiological parameters GSR, HR and RR. The strongest pain-related facial muscle features were the medians of both the corrugator supercilii parameters. The parameters GSR, HR, BR and the two corrugator supercilii parameters of the median matrix correlate more strongly with the level of pain intensity than in the parametric matrix (described in more details in Paper II, Figure 6).

In Sub-study III, the aim was to further investigate the individual role of each feature derived from the five facial muscles in order to develop a feasible and clinically useful EMG measurement as an integral component of the device. The three pain intensities were assessed in more detail and they were subdivided into four time periods: mild pain start (P1), mild pain end (P2), moderate/severe pain start (P3) and moderate/severe pain end (P4) (see Paper III, p.15, Figure 2). The EMG parameters were observed as features of wave length (WL) and the root mean square (RMS) and the correlation analysis was done over the pain periods P1−P4. The activation of each facial muscle feature during test periods was explored using pairwise comparisons of EMG features. The change in activation of all five muscles tested was statistically significant when comparing the P2 and P3 periods, which represent the time when the participant reported the pain threshold. When comparing the five muscles, corrugator supercilii activity increased steadily and most strongly between the periods and were the only ones to show a statistically significant difference ($p<0.05$) throughout the test from the beginning of the stimulus to the pain tolerance. The increase was statistically significant in all test periods, except for the RMS value during moderate/severe pain. The increase in levator labii activity was significant in all tests comparing the periods before and after the pain threshold. The

results for orbicularis oculi activation were similar to those for levator labii, but the feature RMS was not statistically significant when comparing periods P1 and P4. The p-values for Wilcoxon signed-rank statistics are shown in Table 8.

Table 8. Pairwise comparison of both features (RMS and WL) of each tested muscles across the time periods P1–P4. (Adapted from Paper III)

MUSCLE	FEATURE	P-VALUE DURING TIME PERIODS					
		P1 vs. P2	P1 vs. P3	P1 vs. P4	P2 vs. P3	P2 vs. P4	P3 vs. P4
CORRUGATOR SUPERCILII	RMS	0.013	<0.001	<0.001	<0.001	<0.001	0.088
	WL	0.015	<0.001	<0.001	<0.001	<0.001	0.046
ORBICULARIS OCULI	RMS	0.367	0.018	0.057	<0.001	<0.001	0.422
	WL	0.422	0.010	0.008	<0.001	<0.001	0.953
LEVATOR LABII	RMS	0.829	0.001	0.015	<0.001	0.001	0.493
	WL	0.984	0.003	0.022	<0.001	0.001	0.784
ZYGOMATICUS MAJOR	RMS	0.085	0.290	0.570	<0.001	0.023	0.433
	WL	0.164	0.136	0.583	0.001	0.024	0.357
RISORIUS	RMS	0.638	0.023	0.088	<0.001	0.003	0.597
	WL	0.597	0.048	0.071	0.002	0.004	0.456

RMS=root mean square WL= wave form length

5.2.2 The accuracy of the pain intensity classifications (Papers II and III)

The pain prediction model in Sub-study II was done using an Artificial Neural Networks (ANN) classifier. The model was tested separately with the median and the parameter matrix (Table 9). The average classification accuracy of the median matrix was 83.3% and 70.6% in parameter matrix. The results were viewed also as true positive rates (TPR) which were in line with the accuracy of both matrixes. The analysis revealed more modest values in the mild pain class, especially in the parametric matrix. The ROC curves from the overall classification results are shown in article II, Figure 7. The AUC values of the median matrix were 0.90 and over in all pain intensity classes. The AUC of the parameter matrix were also good, with a lower value in the mild pain class.

Because of its lower level of noise and fluctuations, the median matrix classification outperformed the parameter matrix classification in terms of

classification accuracy. Classification using the parameter matrix were still closer to the real-time pain intensity monitoring simulation because the statistical median of each data section was not pre-known.

Table 8. The accuracy and sensitivity of the pain intensity prediction. (Adapted from Paper II)

	MEDIAN MATRIX CLASSIFICATION	PARAMETER MATRIX CLASSIFICATION
DATA SIZE	348.0	12509.0
AVERAGE ACCURACY (%)	83.3	70.6
TPR OF NO PAIN (%)	86.2	70.9
TPR OF MILD PAIN (%)	78.4	65.6
TPR OF MODERATE/SEVERE PAIN (%)	85.3	70.6
AUC OF NO PAIN	0.96	0.91
AUC OF MILD PAIN	0.90	0.78
AUC OF MODERATE/SEVERE PAIN	0.97	0.89

TPR= True positive rate, AUC= Area under curve

According to the results of the correlation analysis of Sub-study II, the physiological parameters HR, RR and BR were those most strongly associated with pain intensity. Thus, these parameters had the greatest influence on the classification performance. The role of facial muscles in the classification result was to be further investigated and in the next step in which all combinations of EMG parameters and their contribution to the classification were observed. The ANN classifiers were trained and tested for each parameter combination. Results showed that adding EMG features to the classifier improved overall performance. However, performance was affected by the approach used to add the parameters. In the median matrix, the best performance was achieved when all EMG parameters were added to the classifier, whereas in the parameter matrix, the AUC value tended to increase with increasing number of EMG parameters.

In Sub-study III, the prediction model was done using the k-Nearest Neighbour algorithm. The selection of most feasible features for the prediction model was done using a meta learning model. The meta learning model tested all possible combination of the ten facial features. A final prediction model was created using the waveform length of corrugator supercilii and levator labii, which were identified as the two most prominent features of pain. The model's performance yielded a c-index of 0.64 which was a modest result but above a value for random prediction.

In the validation of the pain intensity models, the individual differences and the applicability of the model to a new subject were tested using leave-one-subject out cross validation in both sub-studies. The classifiers were trained using data from all of the study subjects but one and then tested with the one subject through the data. The results show, that with the ANN classifier in Sub-study II, for the majority of subjects, the pain intensity was predictable with an average accuracy of more than 70%, and only for four subjects was the accuracy under 50%, while in Sub-study III, the results were more modest, as eight subjects had a c-index > 0.70 and six subject c-index values of 0.43–0.55.

5.2.3 Users' evaluations of the feasibility the Smart Pain Assessment tool concept (Paper IV)

In Sub-study IV, future users were involved in the Smart Pain Assessment tool development. The participants (n=20) in this phase of the study were all registered nurses working in critical care, aged 25−57 years (median 35 years), 85% of whom (n=17) were female. The average work experience of the participants in an ICU was 10.1 years (range 1−30 years).

The attributes of feasible smart technology in pain assessment of critically ill patients

Relative Advantage. The participants identified several potential advantages in using Smart Pain Assessment tool for critically ill patients but at the same time it was identified as an additional device not related to the support of patients' vital functions. The advantages included the optimisation of analgesic use, personalised pain management and possibility learning from earlier pain periods. Participants described that pain medication is frequently administered on a regular and predefined basis, which is often not individualised and situation-specific. The Smart Pain Assessment tool could be used to optimise the use of analgesics, as the effect of analgesics would be easier to detect through continuous pain monitoring. The continuous and more accurate pain assessment enabled by the tool could help to find ways to understand individual needs.

Compatibility. The Smart Pain Assessment tool was identified to be compatible with the currently used pain assessment methods. The current methods were described as including the interpretation of changes in pain-related behaviour and physiological parameters. The detection of the facial changes (expression, pallor, sweating) was an important part of the pain interpretation. Even if many of the detected symptoms are not specific to pain, some of the participants questioned the need for an automated detection device. Moreover, ethical issues related to the use

of objective methods for pain assessment ware raised. The participants were concerned about the possible misuse of the Smart Pain Assessment tool in situations where the tool could challenge the patient's subjective experience of pain. However, pain assessment using an objective measure could also contribute to equal pain management for all patients.

Complexity. In terms of complexity, the participants identified several features that could hinder the use of the Smart Pain Assessment tool. Wearable sensors and wireless solutions were considered user-friendly but not as they were attached to the face. Skin sensitiveness, skin care, potential skin pressure and sensor attachment were also raised. Furthermore, it was also considered that the Smart Pain Assessment tool should be adjustable for individual patients. Participants questioned whether fewer sensors could be used to collect pain-related parameters if not all the sensors could be used.

Observability. Participants described that the results of pain assessment often go undocumented. The results of the pain management process could be observable to others through automated documentation, a clear pain score scale and automated reporting. Specifically, a dedicated module for pain scoring was proposed in the existing patient monitoring screen, as one of the vital signs. This would also ensure a smooth flow of information between those involved in the patient's care and the family members. One possibility to make the presence of pain visible to care staff is the possibility of automated notifications in the smart system.

Trialability. Trialability refers to the possibility of testing an innovation before its wider adoption. Participants' perceptions of their involvement in the process of developing clinical care devices were mainly positive. However, they did stress though that testing technology in their daily work is burdensome. They stressed that involvement in technology development should be part of their normal work and they emphasised their role as nursing experts in equipment development. Implementation of technology developed in collaboration with nurses as the users was considered a more straightforward process.

Smart technology to meet users' need and perceived challenges

Three main categories were formed to describe the perceptions of critical care nurses use of smart technology for pain assessment in critically ill patients who are unable to communicate; *integration of scattered technologies, need for transparent and reliable technology,* and *smart technology as a decision support.* The participants described that nurses in critical care assess pain on a continuous basis but they found accurate and systematic pain assessment challenging. Technology was perceived as both useful and a burden on nursing care.

Integration of scattered technologies. The nurses' working environment in ICUs is highly technological, and the current technology was described as scattered rather than integrated. It was suggested that new devices should to be integrated into the existing patient monitoring and information system, which would also make it easier to use. Integration would also allow access and use of the existing patient data.

Need for transparent and reliable technology. According to participants, it is important to be able to assess the reliability of the data processing, which is done automatically by smart technology. Nurses constantly monitor the condition and well-being of ICU patients using monitors, but they also make judgements about the accuracy of the information provided by the monitors.

Smart technology as a decision support. Technology and the provided information are used as a nursing tool, but nurses also have their nursing expertise. Assessing pain in patients who are not able to communicate, requires various patient observation skills. For pain management, the participants mostly relied on their own observations. Participants described their role in pain management as patient advocates and saw there was sometimes a debate between nurses and physicians about pain management goals. Technology could strengthen the role of nurses by giving them the means to justify their decisions regarding pain management.

5.3 Summary of the main results

In the current study, the preliminary testing and evaluation of the concept of the Smart Pain Assessment tool was conducted. From a technical perspective, an IoT based system was tested using experimental pain. Additionally, the users' needs were assessed and preliminary input for the design was obtained using focus groups. The summary of the main results is presented in Figure 6.

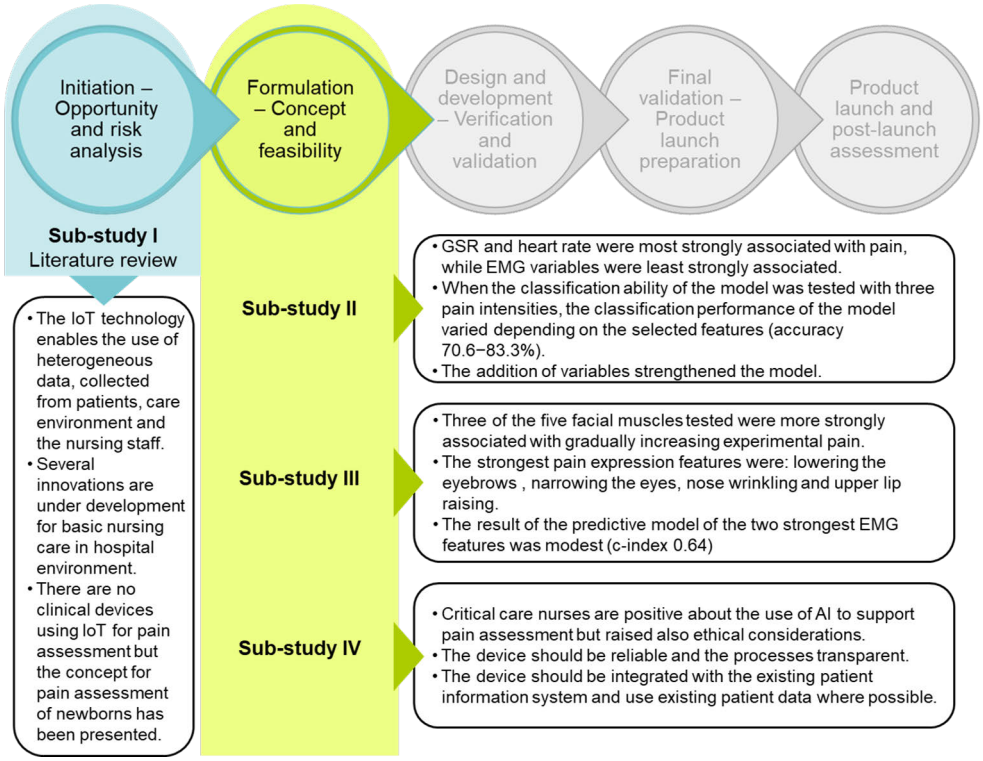

Figure 6. Summary of the main results of Sub-studies I−IV.

6 Discussion

The development of a medical device is ready to move forward in the process as the goals of Phases I and II are reached: These goals include the concept being verified based on the user´s needs and design input, confirmation that it offers customer value, and the technical feasibility is proven and optimised. In practice, the various aspects of the development might be found in the different development phases. (Pietzsch et al., 2009.) The degree of development achieved in this study and the results are discussed in this present chapter as well as the validity and reliability of the results.

6.1 Discussion of the results

Bringing the IoT technology into basic nursing care

In Sub-study I, the applicability and potential of the technical paradigm of the IoT in basic nursing care were examined. The study was conducted in 2016, when the IoT as a technological paradigm was still novel in many sectors. As a phenomenon, IoT is said to have started in 2008, as the number of "things or objects" exceeded the number of people connected to the internet. (Cisco Internet Business Solutions Group, 2011). As the literature review only focused on the hospital environment and basic nursing care, many IoT-based innovations for remote monitoring were not included in the study. The innovations discovered covered a diverse range of nursing topics, although the study found limited innovations supporting basic nursing care. Most of the innovations were related to monitoring patient conditions and activities, but some innovations related to care delivery were also identified.

Only one study was found describing a system based on IoT technology for assessing pain and discomfort. The system was developed for new-borns and was built into an incubator, which was used to obtain heterogeneous data from multiple sources (Martínez-Ballesté et al., 2014). This is an example of an IoT-enabled system that allows the use of diverse sensing technologies and the collection of a wide range of data from patients and the care environment. Assessment of subjective symptoms often remains a challenge, although modern technological advances allow for

increasingly objective and accurate patient monitoring. Assessment is needed to alleviate symptoms, which in turn is essential for the overall well-being of the patient and is associated with a number of care related outcomes (Chanques et al., 2015; Payen et al., 2009). A review by Argüello Prada (2020) on the use of IoT in pain assessment and management supports the view that the development of such systems is still limited and at an early stage. The studies have mainly focused on the development of mobile phone-based pain assessment applications rather than on the development of systems using multimodal physiological data collection and cloud-based computing for data processing and storage.

The added value of IoT is based on fact that an increased amount of information and planning operations can be anticipated and it can be made more efficient by automating the work steps (Rault et al., 2017). However, the research on the effectiveness of the phenomenon in terms of basic nursing care has not yet been carried out. Furthermore, using IoT technology in healthcare poses a number of challenges related to security, privacy as well as education which have to be addressed before implementation. Our findings show that research and development work on novel technologies for basic care work was concentrated in the fields of technology and engineering and multidisciplinary aspects were missing. Several studies call for strengthening the role of nursing in care technology development (Matinolli et al., 2020; Archibald & Barnard, 2018; Glasgow et al., 2018; Castner et al., 2016). In order to shift from a reactive approach to a more proactive stance, the nursing profession must be proactive in anticipating the impact of technology on care. This involves exerting their influence over how technology affects nursing care. (Archibald & Barnard, 2018.)

The proof of the Smart Pain Assessment tool concept

The exploratory testing was done at an early stage of development to assess the initial validity of the concept of the Smart Pain Assessment tool for automated pain detection. A prototype was established to collect easily accessible physiological variables and facial muscle activation using both commercial and research technologies. The results of the physiological variables tested in this study showed that galvanic skin response, respiratory rate and heart rate were associated with experimentally induced progressively increasing pain and these could be feasible variables for the Smart Pain Assessment tool. The strongest single variable was the galvanic skin response, that has also been found to be a valid variable in response to acute pain in clinical settings (Aqajari et al., 2021; Aslanidis et al., 2018; Susam et al., 2018). One of the major concerns with the use of a GSR measurement is that it mainly measures emotional arousal and does not indicate anything about its context; a high GRS value can therefore indicate both a positive or negative experience. Its

use among other variables is recommended, as they can provide information about what caused the emotional reaction. (Gaffey and Wirth 2014.) Another interesting finding is that the respiratory rate decreased during pain exposure, contrary to what has been previously observed in critically ill patients. This may be due to the activation of the parasympathetic nervous system, particularly, when deeper breathing is used as a method of self-regulation (Joseph et al., 2022), which is possible in such test situations. However, this requires further clarification as part of the concept development work. To enhance the use of heart rate as a variable, the inclusion of heart rate variability derived from ECG data could provide additional support, as it has shown promise in the analysis conducted of the same data (Jiang et al., 2017).

While no single physiological parameter is reliable for assessing pain (Devlin et al., 2018; Shahiri & Gélinas, 2023), the variables were combined to a multimodal pain prediction model. The model reached to good average result, as it was able to classify pain with a 83% accuracy, at best, in three pain intensities. The use of multimodal physiological variables to assess pain in critically ill patients also looks promising, as Gelinas et al. (2020) have tested the Nociception Level (NOL) index for pain assessment in critically ill patients with promising results. The NOL index includes several variables, such as heart rate, heart rate variability, photo-plethysmography pulse wave amplitude, skin conductance and temperature. These variables are combined for index using a nonlinear Random Forest regression technique. (Ben-Israel et al., 2013.) The multimodality of the concept was also supported by the result of the ANN classifier, as the performance of the classification was stronger as more features were added to the model. However, contradictory results are also presented: a review by Frisch et al. (2020) shows that at present the multimodal methods are not superior to unimodal pain detection methods.

Facial muscle EMG is an example of a psychophysiological measure used to assess psychological processes and behaviour correlated with bodily physiological processes (Gaffey & Wirth, 2014). The results on the classification of the pain-related EMG features of the facial muscles is modest, which may be partly due to the data collection and prototype related issues, this is discussed in more details in Paper III, chapter 6.2. However, measuring the facial expression with a continuous EMG is one of the core ideas behind the Smart Pain Assessment innovation, as facial muscle activity reflects pain behavior, and distinguishes the device from simply measuring nociception. Pain and nociception are different phenomena and pain cannot be inferred from sensory neuronal activity alone (IASP, 2021). Unlike pain, nociception is not a subjective experience but the result of the physiological encoding and processing of a nociceptive stimulus (Ledowski, 2019).

Five facial muscles were included in this study with aim to assess which muscles provide the most information about pain intensity. Using these results, the number

of muscles measured could be reduced and the method could be developed in a more clinically useful direction. Among the facial muscles, the corrugator supercilii exhibited the strongest association with pain, as it is linked to brow lowering. In addition, the levator labii, responsible for cheek raising and nose wrinkling, and the orbicularis oculi, responsible for eye narrowing, were also found to be connected to experimental pain. The results were promising as they were in line with previous results describing universal pain expressions (Prkachin and Solomon, 2008). As reported by Rahu et al. (2015), most changes in facial expression during pain in critically ill patients were localised to the upper part of the face, where also the muscles corrugator supercilii, levator labii superioris, and orbicularis oculi are located. Therefore, it might be advisable to develop a facial EMG sensor that covers only this portion of the face.

The EMG method is non-invasive, but is generally considered unsuitable for clinical use. Pain expression interpretation in research using the EMG method is also still rare. Only Wolf et al. (2005) have reported a pilot study investigating the activation of nine facial muscles during experimental pain. Automated pain pattern recognition relies almost exclusively on video images, from which facial changes can be decoded by an AU-based frame by frame system. However, Kelati et al. (2022) have succeeded in building a pain prediction model with two facial muscles using the BioVid Heat Database. Facial muscles are small and located in layers and the anatomy of the face can be considered complex. A good knowledge of anatomy is therefore required to position the electrodes on the face in order to measure the correct muscles. (Tassinary et al., 1989.)

The strength of the EMG method lies in its ability to detect the transient and subtle changes in facial expression. The results described in Sub-study II also indicate that changes in facial expressions is transient under continuous, increasing experimental pain, as changes in facial muscle activity were more clearly visible in the median matrix compared to the parametric matrix, which is closer to real-time detection of changes. Kelati et al. (2022) discussed the advances and limitations of surface EMG measurement, with a goal of building an IoT system to automated pain detection. They referred to the ability of continuous measurement to detect facial changes as a strength of the method. On the other hand, signal processing and analysis require specific skills, and movement and coupling can introduce artefacts into the data (Kelati et al., 2022). These issues should be addressed as the development of the Smart Pain Assessment tool continues. In addition, the EMG method may have several advantages in a clinical setting as it does not depend on factors such as patient posture or patient face orientation, unlike the camera-based automated pain detection systems (Nerella et al., 2021). However, these require further investigation and testing in a clinical setting.

Involving the users into the development process

To strengthen the multidisciplinary connection in the development process, the critical care nurses, as the potential users of the Smart Pain Assessment tool were invited to evaluated the feasibility of the concept. Rogers's Diffusion theory of innovation was used as a model to gain insight into the perceptions of critical care nurses of smart technology for pain assessment in the ICU environment. The theory allowed the examination of the characteristics of innovation, focusing on the observed innovation characteristics that increasingly drive further development in a user-centered model (Rogers, 1983). As a result, both the perceived benefits and challenges of the concept of the Smart Pain Assessment tool were identified.

The main advances identified when using smart technology in pain assessment were connected to improve pain assessment which was linked to the optimisation of analgesics use and providing more personalised pain care for critically ill patients. This could be achieved by using a learning algorithm that could use the data from patients' previous pain periods. Decision making in critical care is complex and influenced by the nursing assessment component (Aitken et al., 2009; Wysong, 2014). The assessment of pain in sedated and mechanically ventilated patients is also complex: nurses need to analyse pain behaviour, interpret pain scores, make informed clinical decisions and distinguish between situations requiring analgesia and sedation (Gerber et al., 2015). In cases where patients cannot communicate their pain, nurses' ability to interpret pain-related changes becomes even more important. In the findings, participants expressed a need for a clear pain scoring system through technology, which could enhance current validated observational pain assessment scales. Although the participants identified the potential benefits of Smart Pain Assessment tool, it is currently not sufficiently accurate to provide a clear pain scoring system. While some studies have shown promising results in classifying pain intensities (Hassan et al., 2021), the best that can be achieved at present is pain detection rather than results that can provide a clear pain assessment. The first model developed to classify pain in intensive care patients was binary and used the CPOT scale to classify pain into two categories according to the presence of pain (Kobayashi et al, 2021). While future development may focus on more accurate classification models, the subjective nature of pain makes it difficult to model the pain experience using objective methods.

The inductive analysis also revealed useful information about the possible use and design of the device. Critical care nurses were motivated in using smart technology for supporting pain assessment, but learning how to use new technology and attaching wearable electrodes to critically ill patients seemed burdensome and impractical from the perspective of clinical work. Participants recognised smart technology as an opportunity to utilise existing patient data in a novel manner, thus eliminating the need for separate devices. The study of Kobayashi et al. (2021) has

presented a similar approach, where a semi-automated model was built with data collected from critically ill patients, using the results of physiological measurements and other care-related data. Such an approach needs to be considered in particular in the development of the facial expression detection component which need further development in cooperation with clinical practitioners.

In the results, participants pointed to the need for reliable technology with transparent data processing. Algorithms are frequently described as "black box" models, meaning that the logic and computations behind the resulting outputs are mysterious. It is uncommon for individuals who receive an algorithmic decision to have complete visibility into the data that was utilised to train or test the algorithm, as well as the specific data points that led to the decision. (Morley et al., 2020.) Transparency and the use of methods for explainable AI are prerequisites for the successful implementation for AI in healthcare (Bharatet al., 2023).

Technology or AI itself has no morals or ethics (Einav & Ranzani, 2020; Morley et al., 2020). The ethics of health technology are ultimately determined by their users: when, how and for whom each technology is used (Einav & Ranzani, 2020). In the results from the focus groups, nurses raised ethical issues related to the use of smart technology. The first issue was the potential misuse of the smart technology in a situation where the patient is able to communicate and the pain assessment is inconsistent with patient's self-report. The Smart Pain Assessment tool is not relevant in situations, where the patient is conscious, fully oriented, and able to communicate verbally. The use of the device must be assessed on a case-by-case basis, considering the variability of the patient's mental status. Another issue identified concered the ethical principle that guides pain management, according to which pain should be assessed in all patients regardless of their ability to communicate (Herr et al., 2019b; Raja et al., 2020). Using an automated pain detection method could enable the detection of patients' pain in these cases and improve pain assessment in vulnerable patients.

Critically ill patients experience a number of stressful situations during treatment: common experiences include pain, fear, anxiety, sleep deprivation, tension, inability to communicate, lack of control, nightmares, and loneliness. All these factors can increase the experience of pain according to the biopsychosocial framework (Raja et al. 2020). Symptom management and monitoring is an area of nursing practice that should be developed to improve patient outcomes. (Rotondi et al., 2002.) For the critically ill patients, technology and nurses' expertise are perceived as important because they sustain life functions and enable treatment. However, spiritual aspects such as compassion, encouragement, comforting, alleviating fear and creating safety are the most important aspects of nursing care that patients experienced as support. (Hofhuis et al., 2008.) Physiological and psychophysiological biosignals may be a window into how the human body behaves

under normal and pathological conditions. In the future, psychophysiological measurements and their integration into a multimodal model could promote system management by providing insight into the inner world of patients who are unable to communicate.

6.2 Validity and reliability of the study

6.2.1 Validity and reliability of the data collection

In Sub-study I, a scoping review method was employed, which was suitable for the purpose of mapping the extent and content of research in IoT technology in nursing, as there was available literature with emerging evidence (Peters et al., 2015). The method does not usually include a quality assessment of the included reports (Colquhoun et al., 2014) but such an assessment could have been used to ensure the validity of the included studies. The majority of the included research papers were conference proceedings. Only those studies were included where the technology used was described at a sufficient level to allow its identification as an IoT system. The concept of the IoT is a relatively novel paradigm. The literature search was made across eight databases and was thus comprehensive, but the diversity of the subjects and disciplines resulted also in diversity in the used search terms and strategies. The literature search was not successful with the same search terms in all databases, and the search strategy had to be selected according to the database. This may have led to a loss of systematicity for some databases. Two reviewers were used in the literature selection phase, and their roles were defined according to their disciplinary expertise; one of the reviewers verified that the selected studies addressed the right technology and the other ensured that the research adequately addressed basic nursing care in a hospital setting.

In Sub-study II, a cross-over design was used with four pain tests, two pain induction methods, and several instruments. The use of multiple technical devices to collect data may pose challenges in terms of reliability. However, the data collection was successful, as 116 pain tests (out of a possible 124) could be used in the analysis of the entire pain data in Sub-study II and 120 tests in Sub-study III in the facial muscle analysis. Using a cross-over design with several tests might help control the effect of individual psychological stress in the results. The weakness of the design was that painless control condition (non-painful stimulus) was not used. In addition, when a study participant is subjected to multiple interventions, there is a possibility of a carryover effect (Cleophas, 1993). Randomisation of the pain induction starting position was used to avoid to carryover effect in the analysis.

The study protocol was carefully reviewed and tested several times before the data collection, first with the research team members and later with external subjects.

Data collection was carried out by a technician and two study nurses who took turns in collecting the data. Therefore, there may be some variation in the data collection procedures. The electrical stimulus was delivered using a pre-programmed program on the TENS unit, but the intensity was increased manually every three seconds. This may have led to inaccuracies in the timing of the gradually increasing stimulus. Experimental heat pain has several advantages in research because the spatial location, temperature and duration of the pain stimulus are well controlled (Birnie et al., 2014). The temperature of the thermal stimulus pain element was automatically increased, but the pressure of the thermal element on the skin was not standardised. Heat transfer to the skin is dependent on the pressure at which the heating element is applied to the skin because contact of the heating element with the skin also activates the concomitant non-nociceptors (Reddy et al., 2012).

Due to the pilot nature of the study, the sample size was limited and constrained by the age range of the participants. The sample consisted of working-age volunteers, ranging from 21 to 51. The collected demographics included the age and sex but they were not used in the analysis. Facial expressions of pain have been found to remain unchanged even in older individuals, suggesting that facial expressions are valid measures across age groups (Kunz et al., 2008). However, ageing affects facial structure, and occurs in the facial bones, soft tissues and skin (Farkas et al., 2013). The age should be considered when using EMG to assess pain expression while muscle contraction amplitude and signal selectivity may be affected age (de la Barrera & Milner, 1994; Yun et al., 2014). Electrodes were attached by a designated researcher to each participant according to the instructions of the human electromyography (Fridlund & Cacioppo, 1986), but it cannot be ascertained whether the recorded muscle activities actually reflected the muscle to which the electrodes were to be attached or the adjacent muscle. The crosstalk effect is typical for surface EMG (Farina et al., 2004), especially if the muscles are small and the electrodes are close together, as was the case in the study.

In Sub-study IV, the focus groups were conducted with semi-structured interviews. Two research team members were present for the data collection and they agreed beforehand on the division of tasks. One researcher led the conversation while the other took notes on the course of the interview and the outlines of the discussion. The notes were used to assess the saturation of data collection but not to reflect and verify the mutual understanding with the participants after the interview.

6.2.2 Validity and reliability of the instruments

Several instruments were used in Sub-studies II and III. The instruments were used for experimental pain induction (TENS device, heating element), self-reported pain assessment (NRS), and to measure the pain related parameters (EMG, Bioharness,

GSR measurement tool). The heating element, EMG device and GSR measurement tool were made in house by the research group members with technological expertise. The devices were carefully tested by the research group before use in study, but their validity has not been proven in relation to the pilot nature of the study. The further development of the EMG device has been reported in the study by Sarker et al., (2017). A review of ten studies concludes that the Bioharness device can provide reliable and valid heart rate measurements in a variety of contexts when compared to the gold standard (ECG) and other similar commercial devices (Nazari et al., 2018). In addition, the BioHarness has been proven to be a valid and reliable device for determining breathing rate during exercise (Hailstone & Kilding, 2011). The quality of the biopotential signal poses some challenges to the research. In particular, the EMG sensors had long leads and their movement caused some interference and artefacts with the collected data.

6.2.3 Validity and reliability of the results

Pain is not a single variable, but a state resulting from somatosensory, cognitive and emotional events that changes over time. Its subjective nature is often difficult to assess and interpret objectively. (Giordano, 2004.) Experimentally produced acute pain can be standardised in time and (stimulus) intensity and the mechanisms of production are well known. Even in controlled environment, the experiences of experimental pain can be highly variable both within individuals and among individuals for the same stimulus (Rosier et al., 2002). The participants were aware of the aims of the study to assess the changes in measured pain related behaviour and physiological signs. Pain, especially the pain related behaviours, may be subject to varying degrees of personal control (Hadjistavropoulos & Craig, 2002) which may have affected the results. Furthermore, there is also the possibility that some participants may have exaggerated or tried to control the appearance of pain. The development and validation of an IoT based pain detection system needed data on people experiencing pain. Acute experimentally induced pain served as a starting point for the development of the concept for the Smart Pain Assessment tool. An advantage of the study was that it involved healthy volunteers, thus avoiding the influence of diseases and drugs on the autonomic nervous system. However, a person's experience of pain is influenced by many factors, such as anxiety, expectations and distractions. These are more difficult to influence in experimental studies even though the conditions and measurements are controlled.

The data was explored using various methods including statistical methods as well as two machine learning algorithms. The data was rather small for building such model and lead to the use of same data as a training and testing data. However, effort was used to validate the models using cross-validation and a meta learning model.

The outcomes of classification by machine learning are probabilistic and not sufficient to prove the existence of a causal relationship (Morley et al. 2020).

In Sub-study IV, a purposive sample was used. In a purposive sample, the characteristics of the individuals selected are predetermined based on their relevance to the study's objectives (Andrade, 2021). When using purposive sampling method, the external validity of the study is limited, and the results can be only be generalised to the population similar to used selection criteria. The main limitation of the sample was that it was collected from a single setting. All interviews were conducted in a single level III ICU. The results might possibly have been different if they had been collected from different ICU settings with different levels of care. Another major limitation is that the users in this study only included critical care nurses. Users of medical devices can be defined by specifying the difference between users and end-users (Shah et al., 2008). A user is the person who uses a medical device to treat him/herself or someone else, whereas an end-user is the person who is the ultimate beneficiary of the use of a medical device (Shah & Robinson, 2008). Including patients as end-users, would have strengthened the study and the results should be treated with caution as they do not represent a diverse range of future users.

The Sub-study IV was conducted early in the development process, when the design was in its first prototype phase. The researchers considered that the presentation of the prototype at this stage might have been misleading and may not have corresponded with the intended later design of the device. The concept of the Smart Pain Assessment tool was presented to the participants through illustrations and a verbal presentation, explaining the principles of operation of the device. Participants had the opportunity to ask questions about the device and ensure their understanding, but they did not have the opportunity to see or try out the actual device. This may have led to misunderstandings while discussing the intended use. The semi-structured interview themes were formed mainly from technical point of view to serve the goal of the development of the medical device. With different kinds of questions, for example ones more focused on the pain management process, the results of the interviews could have revealed more insight into actual pain care. As the study has a qualitative nature, these results reflect the experiences and perspectives of the persons who took part in the study. The results are not transferable as such to other settings (Graneheim & Lundman, 2004).

6.3 Suggestions for future research

The following suggestions are made for future research based on these studies:

- In the current study, the early stages of the development process in the Smart Pain Assessment tool are described. The results of the first

explorative validations and feasibility assessments of the concept should be verified with larger samples and with clinical pain.

- The EMG device developed in this study should be validated with an equivalent device that is already validated as a reference.
- The feasibility of EMG method in clinical use should be tested further, as it was used in a laboratory environment and measured while the participants were in static sitting position and were asked avoiding talking. Tests in a clinical health care environment and natural situations should be conducted.
- To ensure the clinical usability of the device, end-users including patients must be involved in the next development phases in a comprehensive way.
- The role of clinical nursing and nursing science in multidisciplinary teams should be strengthened when developing technology for clinical care.
- In similar studies with experimental pain, as well as in the next phases of the current study, the possibility of providing access to pain data for research use should be considered. Allowing other researchers access to data reduces the need to collect similar data, saves resources and is in line with ethical values.

6.4 Implications to clinical practice

Based on the results of the study, the following implications for clinical nursing practice is summarised:

- If the development of the Smart Pain Assessment tool device is successfully completed, it may be useful in detecting painful periods in critically ill patients, particularly those associated with procedural pain and other acute pain, such as post-operative pain. Developing a valid and reliable pain assessment tool for patients unable to communicate may help to provide better physical and psychological comfort in patients who are likely to suffer pain during their daily care. Furthermore, it may help to evaluate outcomes associated with pain management interventions.
- Critical care nurses use technology as a tool to provide care and introducing new technology should ease the work of nurses and not make it more complicated. Nurses generally rely on their own observations of the patient's condition rather than over smart technology and therefore want to be able to assess the reliability of the patient's monitoring equipment.

- The number of new devices needs to be considered when developing technology for the care of critically ill patients. New technology might function better as part of an existing patient information and monitoring system rather than as stand-alone devices.
- The role of nurses in developing technology for clinical nursing is still weak as new technologies are introduced into the area. Nursing professionals should be included in development work, as their perspectives are valuable and they are willing to contribute to development work as users of the proposed care technology.

7 Conclusions

Assessing pain in patients who are unable to communicate is perceived as a challenge that could be addressed, at least to some extent, by the use of smart technology. Automated pain detection is already emerging but there is no clinically usable and validated device for pain detection of critically ill patients who are unable to communicate their pain. The promising progress of this medical device to support pain assessment combining physiological and pain behaviour variables related to acute pain with a learning algorithm should be further developed. Ideally, the development of a device for clinical care should be done at each phase of the development by a multidisciplinary team, and incorporate with users, including both nursing professionals and patients.

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Appendices

Appendix table 1. The literature searches

CONCEPTS	SEARCH	LIMITATIONS
Pain assessment in critically ill patients	((((“pain”[MeSH Terms] OR “pain”[tiab]) AND “assessment*”[tiab]) OR ((“pain”[MeSH Terms] OR “pain”[tiab]) AND “measurement*”[tiab])) AND (((“critical”[tiab] OR “critically”[tiab]) AND “ill”[All Fields]) OR ((“critical”[tiab] OR “critically”[tiab]) AND “care*”[tiab]) OR (“critical care”[MeSH Terms] OR (“critical”[tiab] AND “care”[]) OR “critical care”[tiab] OR (“intensive”[tiab] AND “care”[tiab]) OR “intensive care”[tiab]) OR ((“critical care”[MeSH Terms] OR tiab(“critical”[tiab] AND “care”[tiab]) OR “critical care”[tiab] OR (“intensive”[tiab] AND “care”[tiab]) OR “intensive care”[tiab]) AND “unit*”[tiab])))) AND (pain assessment*)	Adults
Facial expression of pain	((“face”[MeSH Terms] OR “face”[tiab] OR “facial”[tiab] OR “facials”[tiab]) AND “expression*”[tiab] AND (“pain”[MeSH Terms] OR “pain”[tiab])) AND (humans[Filter])	Human
Automated pain detection	(“automat*”[tiab] AND (((“pain”[MeSH Terms] OR “pain”[tiab]) AND (“detect”[tiab] OR “detecting”[tiab] OR “detection”[tiab] OR “detections”[tiab] OR “detects”[tiab])) OR ((“pain”[MeSH Terms] OR “pain”[tiab]) AND (“recognition, psychology”[MeSH Terms] OR (“recognition”[tiab] AND “psychology”[tiab]) OR “psychology recognition”[tiab] OR “recognition”[All Fields] OR “recognitions”[tiab])) OR (“pain measurement”[MeSH Terms] OR (“pain”[tiab] AND “measurement”[tiab]) OR “pain measurement”[tiab] OR (“pain”[tiab] AND “assessment”[tiab]) OR “pain assessment”[tiab])))) AND (humans[Filter])	Adults

Appendix table 2. Literature search results and the included studies

CONCEPTS	PUBMED	CINALH	WEB OF SCIENCE	INCLUDED
Pain assessment in critically ill patients	1025	2218	355	60
Facial expression of pain	895	299/3	588	12
Automated pain assessment	958	688	30	10

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