Touched by technology: automated tactile stimulation in the treatment of apnoea of prematurity

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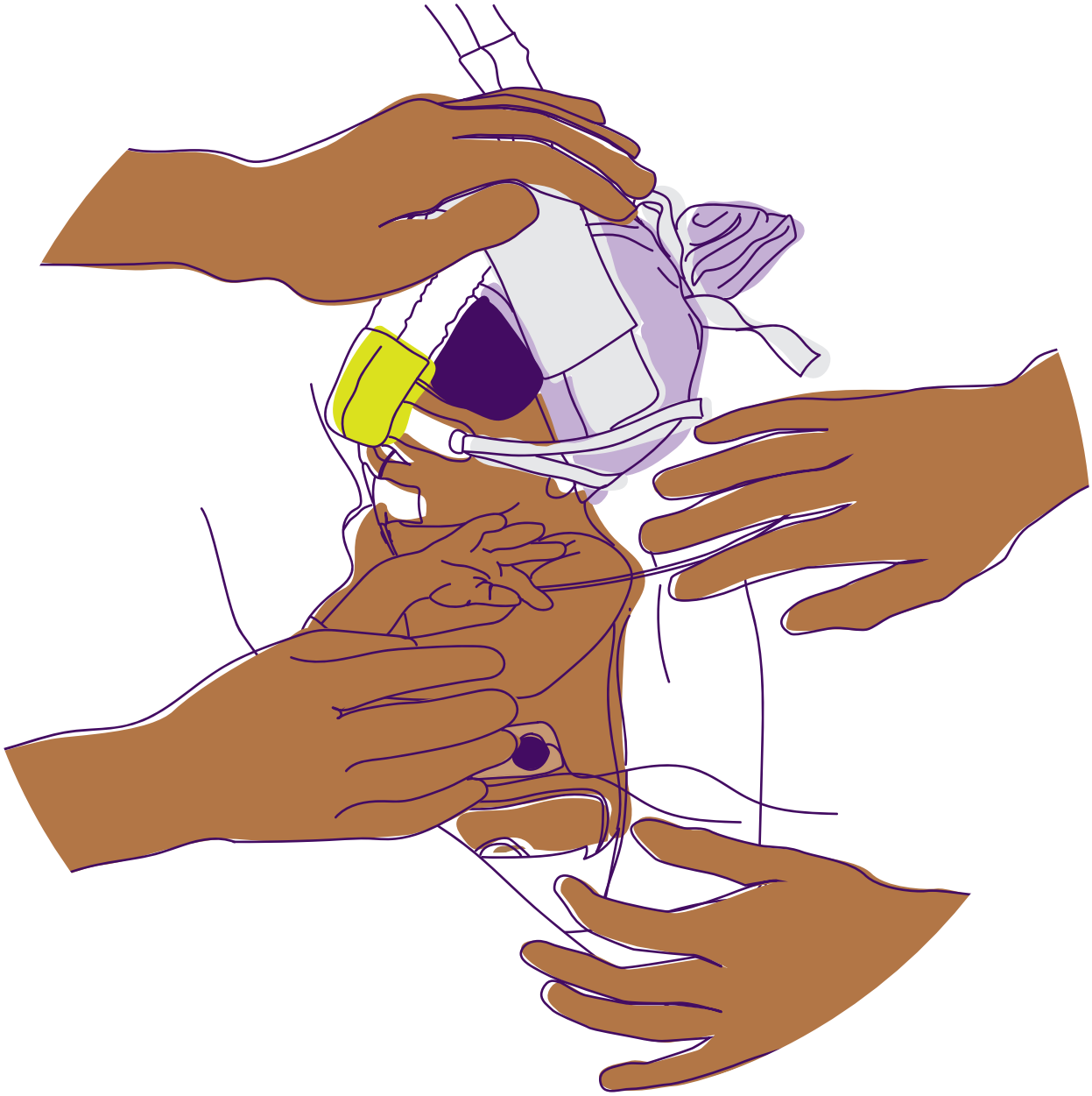

PART 4

CHAPTER 5

Development of the Breathing Operator for BaBY (BOBBY): an automated tactile stimulation device to facilitate breathing in preterm infants

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ABSTRACT

OBJECTIVE

Preterm infants have difficulty breathing unassisted because their lungs and respiratory control systems are immature, resulting in frequent respiratory pauses. Manual tactile stimulation provided by the nurse is effective but also selective and comes with response delays. This prompted us to develop a purpose-built automated tactile stimulation device (ATSD) to address these challenges by providing a reliable and direct response.

METHODS

The development process followed an iterative design approach incorporating five phases. The discover-phase consisted of various studies to gain a deeper understanding of the challenges and context of the problem. The knowledge gained was integrated into user needs and requirements in the define-phase, which in turn provided input for the ideate-phase. Ideas, concepts and prototypes were generated and built during multiple co-creation sessions. Iterative evaluation took place to select the most promising concepts.

RESULTS

Insights from all phases guided the development of Breathing Operator for BaBY (BOBBY), the first purpose built ATSD for preterm infants. In the design, we prioritized safety and efficacy, ensuring separation of electronic components from the infant. We have employed an apparent tactile motion technique, that simulates the stimulation performed by the nurse when responding to cardiorespiratory monitor alarms, to enhance neural excitation while minimizing irritation or damage to the skin.

CONCLUSION

BOBBY can potentially advance neonatal care using automation and address the challenges associated with breathing pauses in preterm infants. Clinical trials are warranted to validate its safety, efficacy and added value in the NICU.

INTRODUCTION

Worldwide, an estimated 15 million infants are being born prematurely each year [1] and this number is increasing [2]. Although the survival rate and overall outcome of these infants have markedly improved over the last decades, premature birth remains the single major cause of neonatal mortality and morbidity in both developed and developing countries.

One of the challenges facing preterm infants is the ability to maintain a rhythmic, stable spontaneous breathing pattern for effective ventilation and gas exchange. Their lungs and respiratory control systems are immature and their control of breathing can be unstable, represented by periods of irregular breathing and frequent periods of apnoea [3]. Although apnoea of prematurity (AOP) is, by definition, an age-specific and self-limiting disorder that resolves with maturation, it can result in adverse events and worse long-term outcomes. The major pathophysiological consequences of apnoea are presumably caused by the accompanying hypoxia and bradycardia, which have been associated with increased mortality, oxidative stress, serious cerebral injury and long-term neurodevelopmental impairment [4-7].

Although existing preventative therapies such as the administration of respiratory stimulants or non-invasive respiratory support are beneficial, most preterm infants still experience respiratory pauses, including apnoea's. To avoid the harmful consequences associated with apnoea, an adequate response consisting of a sequence of interventions is required. This sequence usually commences with tactile stimulation such as rubbing the foot of back of the infant, but can escalate to providing increased supplemental oxygen, positive pressure ventilation and, eventually, intubation [8].

Although tactile stimulation is the first, most frequently used and arguably the most important intervention that has been recommended and applied for years, treatment of apnoea on demand remains an ongoing challenge. Most nurses take care of multiple infants, leading to a large number of tasks and alarms, which requires them to respond selectively and can lead to response delays [9]. Nurses mainly focus on longer apnoeic episodes, as these will increase the risk, duration and severity of subsequent hypoxia and bradycardia [10-12]. However, given their numerical preponderance, brief respiratory pauses also substantially contribute to physiological instability [13, 14] and so are clinically significant and should be treated [15].

We hypothesized that these challenges can be addressed by providing automated mechanical tactile stimulation, offering a reliable and direct response to AOP. Although attempts have been made previously [16, 17], there are currently no commercially available automated tactile stimulation devices (ATSD) that can be implemented in a Neonatal Intensive Care

Unit (NICU). We aimed to develop a purpose-built ATSD prototype by following an iterative design approach.

METHODS

This design project was conducted at the Leiden University Medical Center (LUMC), the Netherlands. The hospital contains a 25-bed level-III NICU divided among two units, with in total 17 single-patient rooms and 4 twin-rooms.

The ATSD was developed by following an iterative design process, containing elements from the Design Thinking methodology of the Stanford d.school, the Stanford Biodesign Innovation process [18] and the Waterfall Method described by the FDA [19]. It consisted of five phases which alternately brought divergence and convergence in the design process (Figure 1): Discover, Define, Ideate, Prototype and Evaluate.

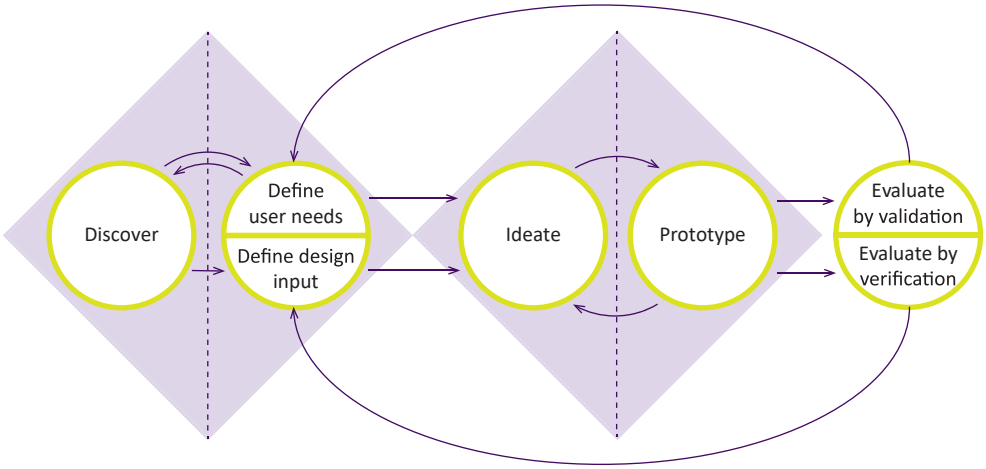


Figure 1. Overview of design methodology that was used for the development of the ATSD

DISCOVER

The goal of this initial phase was to gain a deeper understanding of the problem, the current situation and context as well as greater insights into the needs, motivations and challenges of preterm infants and nurses on the NICU. Several different research methods were used:

1. Several observations were conducted within the NICU. Nurses were shadowed during their shift in order to obtain a better understanding of their routine care practices. These observations were then used as foundational data and provided insights for the development of an interview protocol.

2. In-depth semi-structured interviews were organized with nurses (n=3) and with external experts (n=2). The nurses were selected by the nursing team leader and the questions were focused on the most important aspects of neonatal intensive care and the current AOP treatment process. Both external experts have conducted studies examining the effect of mechanical stimulation on AOP in preterm infants and were asked about their findings, knowledge and opinion on this topic. All interviews were audio-recorded and transcribed for analysis.
3. Two focus groups were conducted in which nurses engaged in a guided discussion exploring how they perform and experience the current treatment process of AOP. The focus groups took place before the start of the evening shift, both times with 8-10 nurses participating. The discussions were audio-recorded and transcribed for analysis.
4. A contextual field study was performed in other to map the stimulation methods nurses currently use, which involved direct observation in a simulated setting. Data collection focused on the location and type of tactile stimulation administered. Subsequently, short semi-structured interviews were conducted with nursing staff to gain further understanding of their rationale behind the chosen tactile stimulation methods.
5. A systematic literature search was conducted to identify the existing evidence for the effects of manual and mechanical tactile stimulation on the termination and prevention of apnoea in preterm infants. Relevant studies were identified through searches of electronic databases and references of the included articles.
6. A preliminary risk assessment was conducted using the Healthcare Failure Mode and Effects Assessment (HFMEA) methodology to identify potential failure modes associated with the concept of an ATSD. The assessment involved a cross-functional team composed of two neonatologists, two nurses, two technicians and one medical engineer.

DEFINE

Based on the first findings of the discover-phase, user needs were identified and functional requirements of the ATSD were defined. By going back and forth between the discover and define-phases in an iterative way, these needs were further specified into design inputs, capturing and defining the intended use of the device and the technical requirements the device must meet.

IDEATE & PROTOTYPE

Guided by the user needs and design inputs, two co-creation sessions were organized by the research team to explore and generate a wide range of potential solutions. Both sessions took approximately 1.5 hours and were attended by one or two NICU nurses, one neonatologist, one researcher, two technicians and two (medical) engineers from our hospital. In between and after the two brainstorm sessions, there were many smaller half-hour sessions in which the technician and engineers discussed the technical possibilities and feasibility of the concepts. All sessions were followed by the development of prototypes, which were tested against the predefined requirements to select the most promising design direction or concept. In this way, the design was further fine-tuned by each session.

EVALUATE

In addition to the iterative evaluations of concepts and prototypes, the final design was verified by evaluating whether all predefined design inputs were met, using different tests and checks. Final validation will occur in the future as it requires clinical evaluation and so will not be included in this report.

RESULTS

The results from the abovementioned phases served as input for the ATSD. Below we provide a description of the accompanying findings of each phase and a description of the final design.

DISCOVER

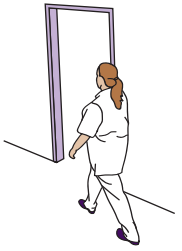
The observations from the NICU and information derived from interviews and focus groups resulted in a broad overview and deeper understanding of the NICU environment, important aspects in the care for preterm infants and the current treatment of AOP (Figure 2). In addition to the insights from the treatment process, the following items were taken into account: (1) preterm infants are placed in incubators in order to provide a warm and humid environment, (2) preterm infants are extensively monitored and supported by variety sensors and devices, such as pulse oximetry sensors, ECG leads, phototherapy devices and intravenous (IV) lines, (3) preterm infants often require medical interventions and checks such as line placements, IV insertions or routine ultrasound examinations and (4) preterm infants benefit from skin to skin contact with parents.

Figure 2. Overview of and insights from the current apnoea treatment process

Be alarmed
Alarms are visible and audible on the patient monitor in question and at the central post. A selection is transferred to the pager of the nurse to minimize alarm fatique.

The nurse will accept the alarm on their pager if he/she has time and otherwise try to actively deny, so the alarm will be redirected immediately to a buddy nurse. In case the nurse does not respond within 30 seconds, the alarm will be redirected automatically to ensure a timely response.

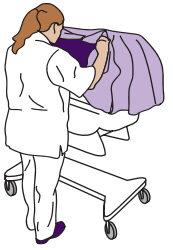
To ensure a timely response, nurses must actively decide to acknowledge the alarm or not and are therefore always interrupted. For caregivers there is a fine line between clinical awareness and alarm fatique.



Decide to act
The nurse who accepts the alarm will consider whether to act or not, depending on amongst others the event type and severity, the course of previous events the clinical status of the infant.

In most cases the nurse will wait and (remotely) monitor the patient for a while to see whether the event is brief and self-resolved or if intervention is required.

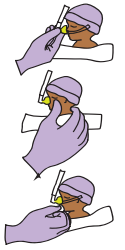
Nurses can only respond to a selection of events and are usually not in the position to respond immediately. In addition, nurses try not to disturb the infant unnecissarily.



Find the cause
At the bedside the nurse will silence the alarm, open the cover and turn on the light above the incubator to inspect the infant and find the possible cause for the event.

This involves inspecting the thorax on breathing movements, the respiratory support interface on pressure leaks, the position of the head for possible obstruction, the skin colour for signs of reduced blood flow or oxygenation and the mouth for vomit or mucus. If it is hard to see, the incubator is opened and the blanket is removed or the infant is slightly turned over.

Finding the cause of the event already disturbs the infant in the form of sound and light.



Intervene
In some cases cleaning the mouth, replacing the respiratory support interface or replace the head is a sufficient remedy. However, if the event is very serious or there is no evident cause for the event, the nurse will apply tactile stimulation. FiO2 is automatically controlled based on the oxygen saturation.

If stimulation does not help, the nurse will turn the infant around to ensure arousal. Ultimately, if all attempts fail and no progress is made, the nurse will call assistance and ventilate the infant. In the worst case, the neonatologist will intubate the infant.

Nurses use different interventions depending on the cause of the event but tactile stimulation is the most applied intervention.

Report
Most of the nurses only report events where they had to intervene. Based on their observations and data from the patient monitor they mark an event as an A (apnea), B (bradycardia), C (cyanose) or a combination.

The documentation is used by both doctors and nurses to keep track on the status of the infant over a longer period of time. Details about the events, the assumed causes and the response to the interventions are shared during the handover with the next nurse on duty.

Events are reported manually, resulting in subjective and potentially inconsistent clincial references.

Our contextual study showed that the tactile stimulation approaches currently used by nurses are highly variable, particularly the stimulation technique and the targeted locations on the infant's body [20]. We observed ten different stimulation techniques, with the application of pressure or the rubbing of skin the most common, which were mainly applied to the torso (thorax, side or abdomen). Stimulation methods were based on either prior training or intuition, which is a logical consequence of the lack of evidence-based recommendations.

A systematic literature study revealed that several systems and devices have been developed to provide mechanical and automated intervention of AOP [21], again with large variations in stimulation characteristics. Studies focusing on the termination of apnoea showed that this is possible with a closed-loop mechanical pulsating or vibrating device and that mechanical vibratory stimulation of 250 Hz is equally effective as manual stimulation. Studies investigating the effect of tactile stimulation on the prevention of apnoea mainly used oscillating or vibrating stimuli, the latter of which showed the best results by consistently reducing apnoea, hypoxia, and bradycardia. The added value of a direct response however remains unclear as there are no comparisons between automated systems and the current manual approach. Similarly, the most effective form of tactile stimulation is unclear, which stems from the lack of knowledge about the exact working mechanism and the sensory neuronal pathways. These findings were confirmed in the expert interviews.

Finally, the preliminary risk assessment for an ATSD, regardless of its design and shape, identified 7 general risks that need to be considered during development. These included: (1) risk of electrical shock of patient/user, (2) risk of skin damage, (3) risk of interference with other devices, (4) risk of hampering breathing, (5) risk of overstimulation/agitation, (6) risk of habituation and (7) risk of cross contamination/infection.

DEFINE

Initially, we defined five important user needs that the ATSD should fulfil to be of added value. These included; the device should (A) provide effective automated mechanical stimulation, (B) be safe, (C) suitable for preterm infants at risk for AOP, (D) user friendly and (E) maintain clinical awareness of the nurse. These user needs were further broken down in technical requirements originating from the findings of the discover-phase (Table 1).

As there is currently no standardized stimulation method that has shown to be effective, we will have to demonstrate that our device provides stimulation that is at least as effective as that provided by a nurse. As a result, a protocol for clinical evaluation was developed in parallel with the list of requirements, which was adapted accordingly. In order to perform this evaluation it must be possible to assess whether and when tactile stimulation (either

manual or mechanical) has been applied; a sixth user need that the ATSD should meet (F, Table 1).

As is it not yet possible to accurately predict cardiorespiratory events, we decided that the ATSD should respond to the clinical alarms the nurses receive. This enables evaluation of the effect of a direct response without affecting the initiation of alarms and thus the clinical awareness of the nurse.

IDEATE, PROTOTYPE & EVALUATE

In both brainstorm sessions, brainwriting and braindrawing were used to come up with solutions to a variety of problems. These included; (i) identification of existing devices that can provide tactile stimulation (e.g. toothbrush, game controller, massage chair and blood pressure cuff), (ii) clarification of the different forms of tactile stimulation that can be applied (e.g. pulling, pressing, stroking, massaging, tapping, squeezing, scratching, vibrating and shaking), (iii) different techniques for providing tactile stimulation (f.e. vibration motors, speakers, air pulses, squeezing inflatables, rotating balls in bearing, rolling cylinder and waterbed) and (iv) different ways to attach stimulating devices to a preterm infant (f.e. sticking or sucking to skin, clamping, knotting or clicking to diaper, ECG sensors, mattress, blankets or the incubator itself or keep in place by gravity). The ideas were combined into concepts and prototypes, ranging from simple sketches at the start to detailed physical models at the end, and were evaluated and compared through discussion with nurses using a selection of requirements (Table 1). Finally, several different test methods were used to verify that the final design met all the technical requirements specified (Table 1). This confirmation served as input for formal clearance of the ATSD for clinical evaluation, which was granted.

END RESULT

The final version of our ATSD, called BOBBY (Breathing Operation for BaBY), provides automated vibratory stimulation on the thorax of the infant directly after the onset of a clinical alarm from the patient monitor. BOBBY consists of multiple parts that are connected to each other in the following order: (1) a light sensor placed on the patient monitor, (2) a control-box consisting of a mini computer (Raspberry Pi 3, Raspberry Pi Foundation, UK) a camera and infrared lights placed on the back of the incubator, (3) an activation-box, housing an amplifier and two speakers placed near the incubator (4) a silicon strap with integrated air cavities placed on the thorax of the infant and (5) a fabric belt with small pieces of Velcro that keeps the strap in place (Figure 3).

Table 1. List of requirements including user needs (A-F) and underlying technical requirements, origin and purpose.

	Description	Origin	Purpose
A	**Provide effective automated mechanical stimulation**		
1	Start stimulation at onset cardiorespiratory alarm	Study protocol	Verification: bench test
2	Stimulate the thorax	Contextual study, interviews	Verification: physical check
3	Enable variable stimulation intensity/frequency	FMEA: risk of habituation	Verification: bench test
4	Enable stimulation site alteration	FMEA: risk of habituation/skin damage	Verification: physical check
5	Gentle stimulus	Focus group, interviews	Concept comparison
6	Stimulate large area	Focus group, interviews	Concept comparison
B	**Safe for preterm infants at risk for AOP**		
1	Stop stimulation at end cardiorespiratory alarm	FMEA: risk of overstimulation/agitation	Verification: bench test
2	Electrically safe according to IEC60601	FMEA: risk of electrical shock patient/user	Verification: electrical safety test
3	Electrical parts completely insulated	FMEA: risk of interference other devices	Verification: electrical safety test
4	Non-sticky material	FMEA: risk of skin damage	Verification: physical check
5	Soft material with rounded edges	FMEA: risk of skin damage	Verification: physical check
6	Medical grade material	FMEA: risk of skin damage	Verification: material documentation check
7	Temperature of device <38°C	FMEA: risk of skin damage	Verification: endurance test with temperature check
8	Resistant to disinfection according to hospital standard or disposable	FMEA: risk of infection	Verification: material documentation check
9	Noise within incubator <45dBA	FMEA: risk of agitation/discomfort patient	Verification: sound test
10	Minimal pressure when stimulating	FMEA: risk of skin damage, hampering breathing	Concept comparison
11	Minimal pressure when not stimulating	FMEA: risk of skin damage, hampering breathing	Concept comparison
12	Minimal contact area	FMEA: risk of skin damage	Concept comparison

	Description	Origin	Purpose
C	**Suitable for preterm infants at risk for AOP**		
1	Fits on infants of 23-38 weeks gestational age	Target group	Verification: physical check
2	Fits in/on an incubator or crib	Focus groups, observations	Verification: physical check
3	Resistant to temperatures of 20-50 degrees	Focus groups, observations	Verification: Endurance test
4	Water resistant	Focus groups, observations	Verification: bench test
5	Resistant to 80% humidity	Focus groups, observations	Verification: bench test
6	Fits in combination with sensors/lines/breathing interfaces	Focus groups, observations	Concept comparison
7	Works during kangaroo care	Focus groups, observations	Concept comparison
8	Works during ultrasound examination	Focus groups, observations	Concept comparison
9	Works during placement of lines/IV	Focus groups, observations	Concept comparison
10	Minimal blockage of phototherapy	Focus groups, observations	Concept comparison
D	**User friendly**		
1	Max two additional wires	Interviews, observations	Verification: physical check
2	Attach/detach to the infant within 10 seconds	Interviews, observations	Verification: User test
3	Set up at bedside within 3 minutes	Interviews, observations	Verification: User test
4	Easy to transport	Interviews, observations	Concept comparison
5	Easy to use and understand - minimize amount of settings	Interviews, observations	Concept comparison
6	Minimize cleaning time	Interviews, observations	Concept comparison
7	Minimize total size	Interviews, observations	Concept comparison
E	**Maintain clinical awareness**		
	N/A		
F	**Asses applied interventions**		
1	Log start and end of stimulation	Study protocol	Verification: bench test
2	Videorecord inside incubator	Study protocol	Verification: bench test

The work flow for BOBBY commences with the detection of a clinical alarm, usually a flashing light on the patient monitor, which is detected by a light sensor. Upon detection, the computer activates both speakers by playing an audio file, causing the cones of the speakers to oscillate. The speakers are airtight connected to two thin-walled air cavities in a silicon strap, positioned on the infants skin. The pressure signal of the speakers is transmitted via silicon tubes to the air cavities, which start to vibrate and stimulate the infant's skin without producing sound. In addition to the stimulation, the computer also activates the camera, capturing a video of the inside of the incubator. The videorecording is stored on the computer and the start and end time of the stimulation is logged to enable evaluation of the intervention afterwards.

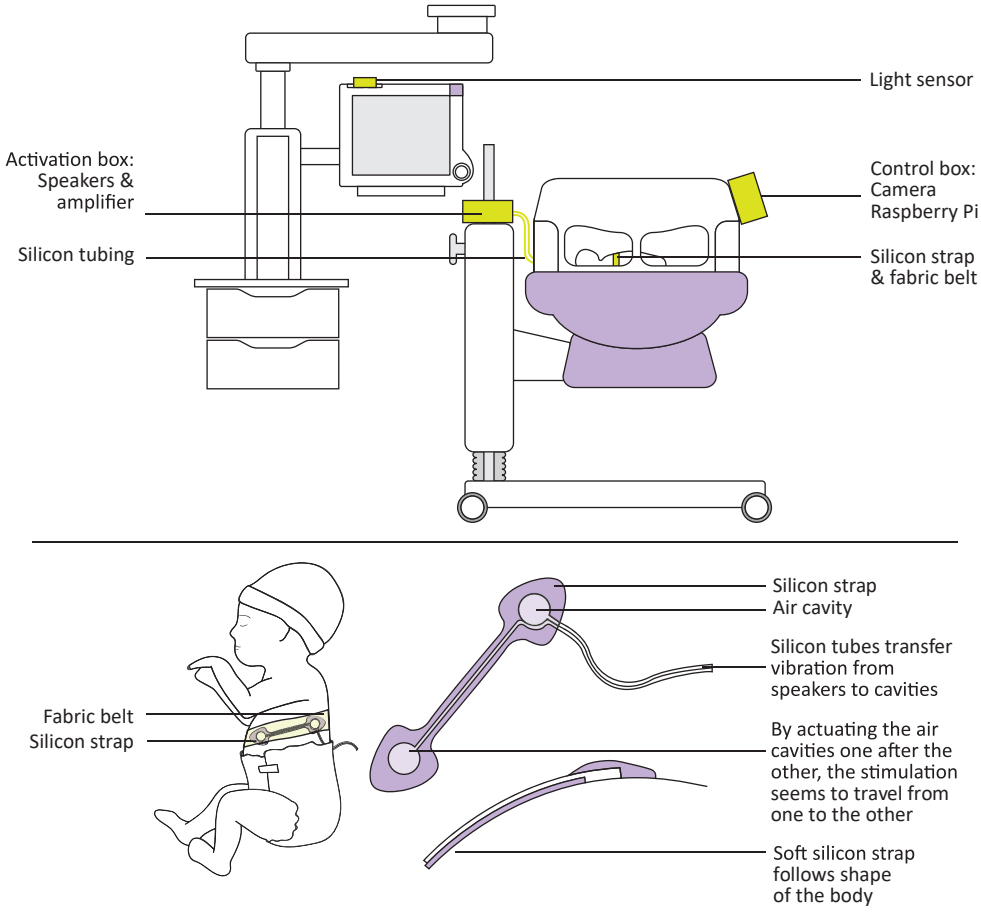


Figure 3. Overview of set-up and embodiment of BOBBY

The distinctive features of BOBBY include the activation of stimulation using speaker-like pressure actuators, enabling separate amplitude and frequency control. It also allows the separation of electronic parts from the incubator, preventing possible heat, electrical or acoustic injury to the infant. Furthermore, the soft and flexible strap that is easily attached, detached and replaced, makes BOBBY usable in different scenario's including kangaroo care. However, the ingenuity of the design is mainly in the way the stimulation is provided. In order to stimulate a large area of the skin without the need for a large and cumbersome probe, BOBBY provides apparent tactile "motion" [22], which provides the sensation of vibration that travels in a continuous motion from one actuator to another. This illusion is created by controlling the length and delay (onset asynchrony) of actuation between the two pressure actuators. This implies that once an alarm is detected, the computer first activates one speaker and then the other after a varying delay. As a result, the infant will experience a soft stroking sensation underneath the silicon strap, moving from the position of one cavity to the other.

BOBBY is patented under EP4103042A1 [23].

DISCUSSION

Although the idea of using mechanical and/or automated tactile stimulation to reduce or shorten breathing pauses in preterm infants is not new, our approach and development process is unique. These previous studies primarily applied existing tools [11, 16, 17, 24, 25], whereas we developed a device specifically for the application by using an iterative design process. This ensured that factors such as user needs, contextual requirements and potential risks were considered in the early stage and continually reconsidered, directing the design of a safe, effective and desirable solution.

The biggest challenges for developing this device were defining requirements and making design decisions regarding the effectivity of the stimulus, caused by two main obstacles: (1) despite existing evidence of tactile stimulation to (re)initiate breathing, the precise mechanism of action and therefore the most effective way of stimulation are unclear and (2) conducting explorative or interim tests of various ways of stimulation in preterm infants to enable quick iterative steps were not feasible due to ethical and safety considerations.

Rather than starting fundamental research to find out the mechanisms of action, we opted for a pragmatic approach and drew insight from existing literature, clinical experiences and expert opinion to design a device that is most likely to be effective. Additionally, we retained flexibility in the design (e.g., the ability to adjust amplitude and frequency independently) to allow for further refinement of the stimulus through future clinical research.

Although we used several research methods to gain insights into the problems and potential solutions, the process was limited by the fact that nurse input came from a relatively small group of people from our own ward. Furthermore, parents of preterm infants were not yet included in the developmental process, as the primary goals was to establish a scientific foundation for the design. However, recognizing the important role of parents in the eventual success and usability of the design, we plan to involve them in future iterations of the device. Although the device is currently tailored to function correctly in our department in order to evaluate its safety, feasibility and effectiveness, we believe the concept of BOBBY can be easily refined to make it suitable for other units and accepted and embraced by parents.

Assuming its stimulation is equally effective as manual stimulation, BOBBY will be able to reduce BRP's and apnoea and thereby reduce the onset or exacerbation of associated hypoxia and bradycardia by providing an automated and direct response. In the future, combining BOBBY with a predictive algorithm may provide a preventative solution that potentially avoids cardiorespiratory instability in this vulnerable cohort of infants. By logging and visualizing the required tactile intervention in the future, BOBBY could also aid objective clinical assessment of the infant and therefore benefit both patient and nurse.

CONCLUSIONS

We aimed to address current challenges in the treatment of breathing pauses in preterm infants by developing an automated tactile stimulation device that enables a direct and reliable response. This was accomplished using an iterative design process, culminating in the creation of BOBBY, which is a novel stimulation device that is ready for clinical validation. Ultimately we consider that it will be integrated in standard neonatal care.

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