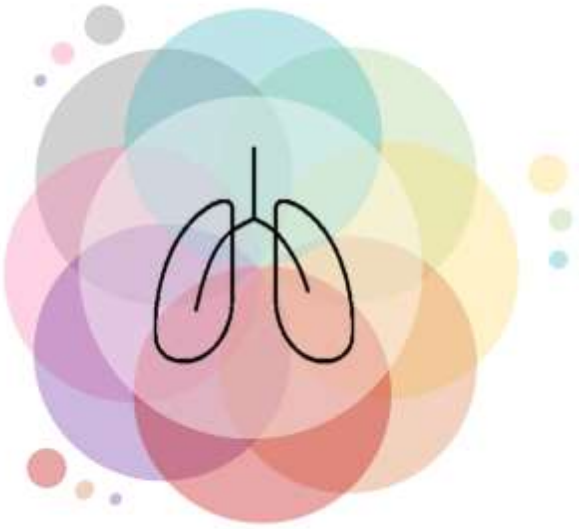

BreathX – Stressfree Radiotherapy

Audio-visual feedback to gently guide patients through radiotherapy

Whitepaper

Project Team

Anna Magdalena Springer, BSc., Samuel Baumgartner, BSc., Judith Höllebrand, MSc, Lisa Meneder, BSc, Kerstin Prock, BSc., Theresia Schauerhofer, BA.

Project Coach

FH Prof. Jakob Doppler, MSc.

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1 Radiotherapy using DIHB for mamma-carcinomas

In Austria one in eight women is affected by mamma carcinoma (Gnant et al., 2018). In 2017 about 5.417 new cases of mamma carcinoma were reported according to Statistik Austria, this corresponds to 30% of all possible cancer types women can get. The therapy of mamma carcinoma depends on the individual case but overall most patients undergo a radiotherapy (Gnant et al., 2018). Radiation therapy uses ionising radiation to target tumor cells, which are more sensitive to radiation than healthy tissue. A tumor board (a team of specialized doctors) is used to determine the general therapy and the tumor stage. The radiation plan determines which area will be irradiated with which radiation technique and dose and how many sessions. Care must be taken not to exceed certain dose limits of the organs at risk to prevent the likelihood of side effects. For this reason, respiratory triggering is used for left-sided breast CA. Beforehand, the radiation plan is drawn up by means of a CT in the exact same position of the patient as then used for RTX, in order to be able to plan as precisely as possible.

Nowadays left sided mamma carcinomas are treated with the DIBH-technique at the radiotherapy (Corradini, 2017). During radiotherapy including deep inspiration breath hold (DIBH) technique patients must hold their breath for as long as possible in the required breath hold area to start the treatment. Figure 1 shows how radiotherapy with the DIBH technique works: As soon as the breathing curve is not in the required blue area, the radiation beam automatically stops (Bergom et al., 2018). The patient has to repeat this as often as needed to achieve the individual dose in the tumor tissue.

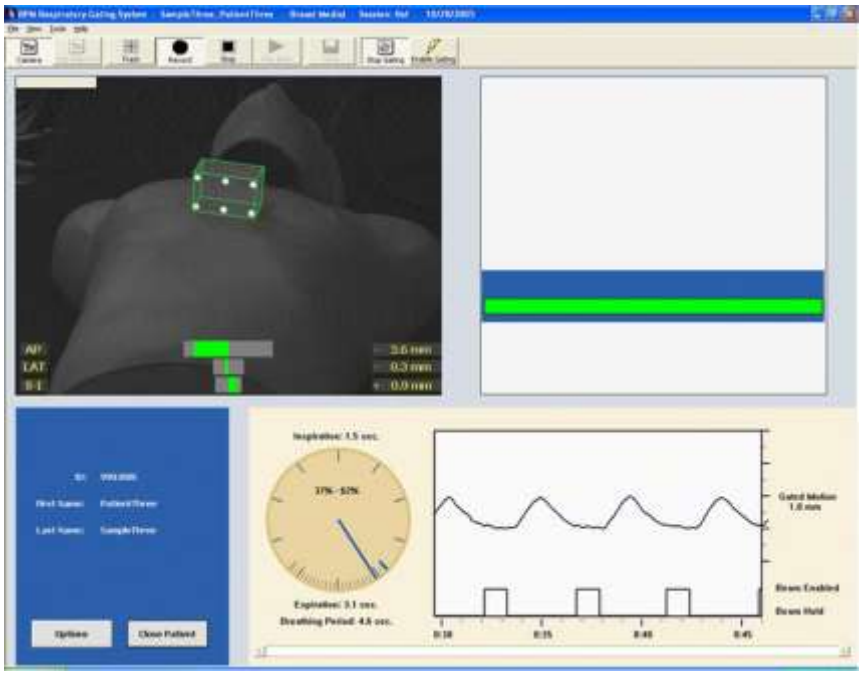

Figure 1 real time position management (Moorees & Bezak, 2012)

2 What is BreathX and why do we need it?

The DIBH-Technique is used to minimalize the doses of organs at risk. Generally, organs have a specified maximum dose which they are allowed to get without arising critical side effects. The problem concerning left sided carcinomas is, that the heart and lots of lung tissue will be in the treatment field during radiotherapy. This can cause ischemic heart disease, lung fibrosis, radiation pneumonitis and many more side effects (Corradini et al., 2018).
The relative risk of a major coronary event increases per gray mean heart dose with 7,4 %. As mentioned above it is also possible to harm the lung tissue. The radiation can lead to secondary lung cancer. Therefore, it is important to keep the mean dose as low as possible to prevent radiation-induced heart or lung diseases (Rice et al., 2017). Due to the DIBH-Technique the doses of the normal and healthy tissue will be minimalized which also evokes a decrease in side effects (Corradini et al., 2018).

As said in chapter one, when using the DIHB-Technique a breathing curve including a breath-hold-area is visualized to show whether the patient's chest is in the right position. The radiographer can see the respiratory curve, but the patients themselves cannot. Therefore, the radiographer must guide the patient to the required breath hold area, using instructions. This takes a lot of time and can be stressful for the patient as well as the radiographer.

The quality of current radiotherapy for left-sided mamma-carcinoma patients is lacking in terms of visual-auditive feedback. BreathX can solve this problem by supporting patients during radiotherapy using visualization and auditive techniques. In doing so, the work of the radiographer is simplified, and the treatment takes less time. The prototype gives helpful audio-visual feedback to the patient and gently guides him/her through every radiotherapy session. It helps the patients to better understand their breathing curve, while at the same time creating a relaxing atmosphere based on scientific methods.

3 BreathX - The prototype

The system currently in place ceases radiation treatment as soon as deviation from the predetermined breathing curve is detected. This evaluation is only accessible to the radiology technician but not the patient. The prevailing lack of communication creates a clinical need for improved patient feedback which we provide with our prototype. In the following the most

important findings concerning visualization and auditive feedback are summarized. Based on these findings we designed our prototype. For more details and evidence see chapter 4.4.

3.1 Visualization

At the moment there are only audio instructions for mamma irradiation used, although studies show, that additional visual instructions provide positive effects for breathing therapy. Patients reported they were able to focus on breathing better when provided with visual instructions and trainings were also reported to be more accurate (Blum et al., 2020; Chittaro, 2014).
In general, there are two typical visualization methods for the breathing curve. One of those methods are growing circles, which indicate patients if they should inhale, hold the breath or exhale (*Figure 2*). The other one is as waves, like you see in the *Figure 3*.

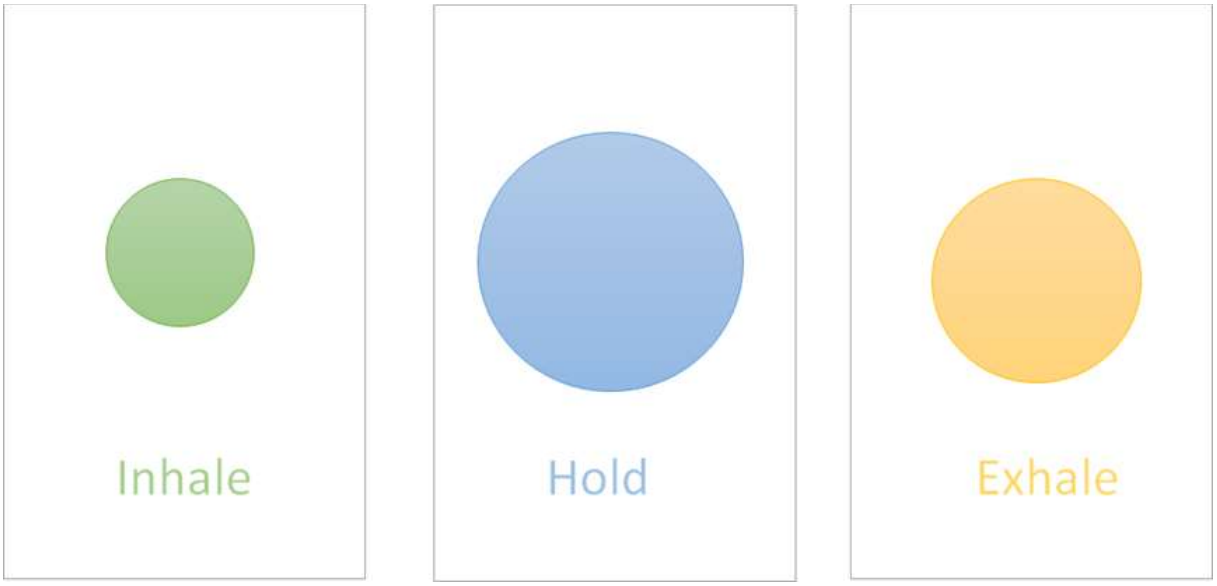

Figure 2 Breathing visualization as growing circles

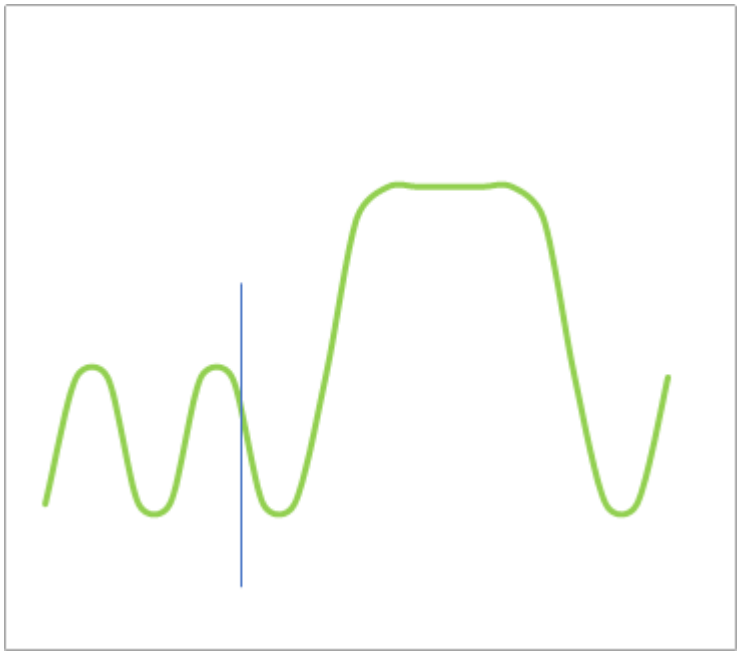

Figure 3 Breathing visualization as waves

Chittaro (2014) compared both methods and reports a slight preference for waves because the entire breathing cycle is already visible. Most important for breathing therapies is that patients can optimally focus on breathing. Therefore, Patibanda and colleagues (2017) suggested minimalistic designs, relaxing surroundings and not too many distractions. To achieve good concentration on their breathing it is helpful for patients to have naturalistic surroundings like a green island or floating water as well as getting feedback during breathing exercises (Patibanda et al., 2017).
Overall, there are big differences between visualization preferences (Zhu et al., 2017). That is the reason why in this project, more than one naturalistic design was developed, so patients can choose the most relaxing one for them.

3.2 Audio

Multiple studies show that the procedure of a radiotherapy causes stress, frustration, depression and fear in breast-cancer patients. To reduce these symptoms and create a relaxing and calming atmosphere music intervention represents an effective and safe method (Nardone et al., 2020; Rosetti et al., 2017; Chen et al., 2020).

Gramaglia et al. (2019) and Rosetti et al. (2017) observed a strong and significant reduction of stress, depression and anxiety through music intervention during radiotherapy.

Furthermore, a significant stress relieving, and relaxing effect was reported by using auditory alpha activity training in a range of 8-12 Hz. An increase of ten percent in alpha activity in posterior sites occurs (van Boxtel et al., 2012).

3.3 Our Prototype

There are certain technical and functional requirements which a system guiding a patient's breathing cycle must abide to. One main point being that any technical installation must not interfere with the normal proceedings within the radiotherapy room. The system should be as unobtrusive as possible, ensuring that interference with the clinical work environment is kept at a minimum. It should also be easy to operate for the medical personnel. Furthermore, the design and the audiovisual feedback must be kept intuitive in order to be understandable for patients, regardless of age or any previous technological knowledge.
Another major point to be taken into consideration is the overall cost of such a system. A relatively low initial acquisition cost can serve as an incentive for potential customers.
Real Time Engine-Environments such as VVVV or similar visual programming languages like MAX/MSP/Jitter can produce processing intensive results quite quickly. Therefore, a balance between computing power and cost will have to be struck. Equipment such as video projectors and audio devices will have to be factored into the cost as well.

Due to the pandemic, we did not have the chance to build our prototype in a real-life setting. Normally a plastic cube with reflecting stickers is placed on the patient's chest, when breathing the plastic cube goes up and down with the movement of the chest. This movement is detected by an infrared camera, that sends the data to a software where the breathing curve is visualized for the radiographer.

For our prototype we used the Azure Kinect by Microsoft to measure the breathing-movement (figure 4), that we connected to VVVV.

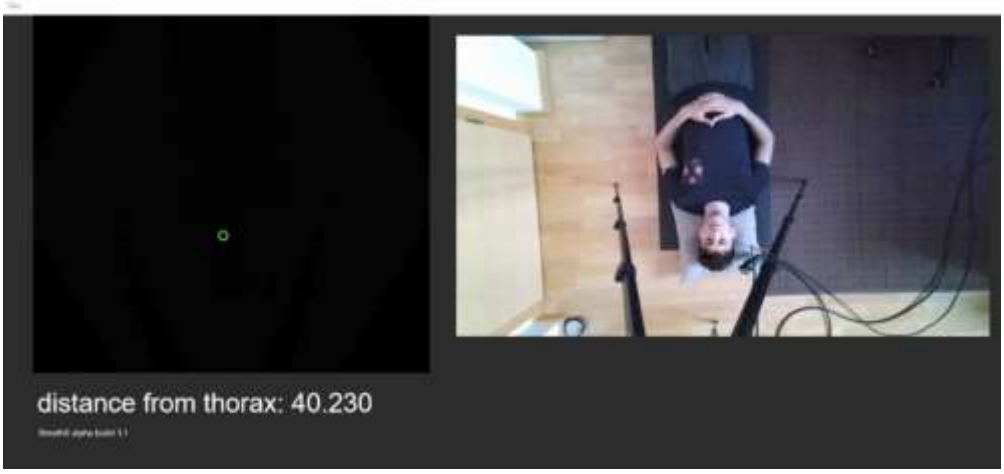

Figure 4 Azure Kinect Breathing Detection

In VVVV we built an environment to visualize the breathing curve (figure 5). We chose a relaxing visualization, as can be seen in figure 5. The balloon rises and falls with in- and exhalation. The goal is for the balloon to rise to the height of the dark grey bar.

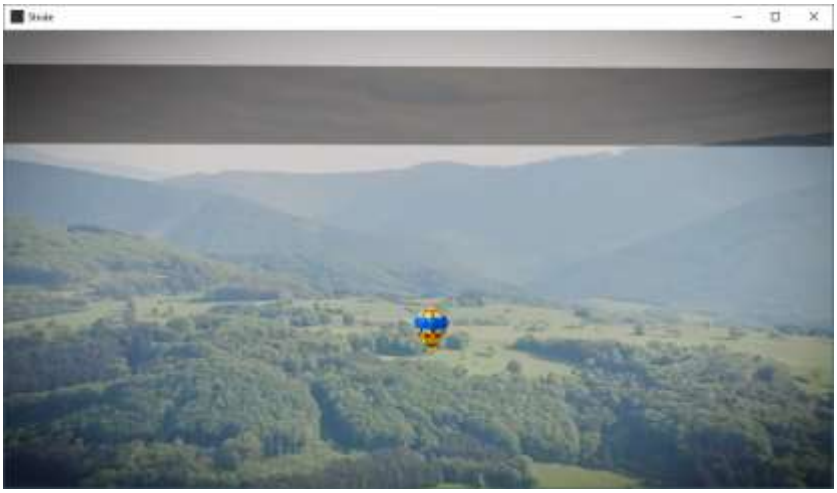

Figure 5 Visualization 1

As soon as the balloon is completely in the dark grey bar, it turns green (figure 6). This provides an additional visual feedback for the patient, symbolizing that the inhalation level is right and that they now should hold their breath for as long as possible to trigger the radiotherapy. We also provide auditive feedback – a bell chimes when the bar turns green. When the patient exhales the balloon falls and leaves the bar – it turns from green to dark grey again.

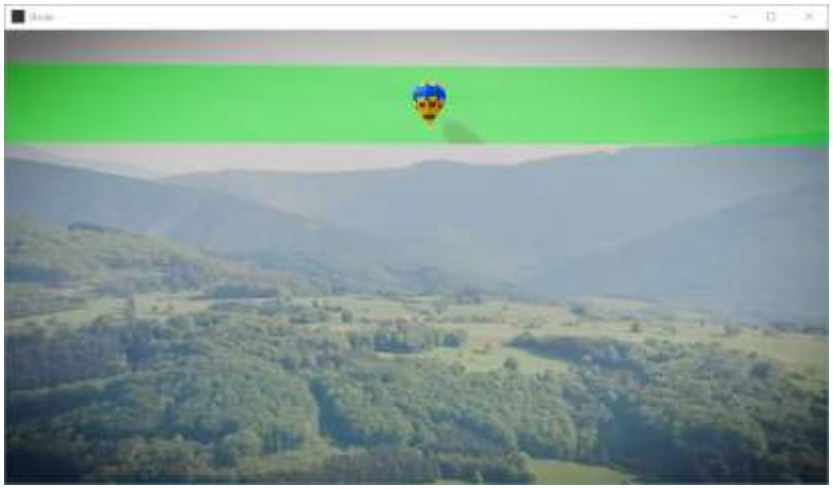

Figure 6 Visualization 2

n figure 7 the implementation of the depth sensor of the Azure Kinect in VVVV is shown.

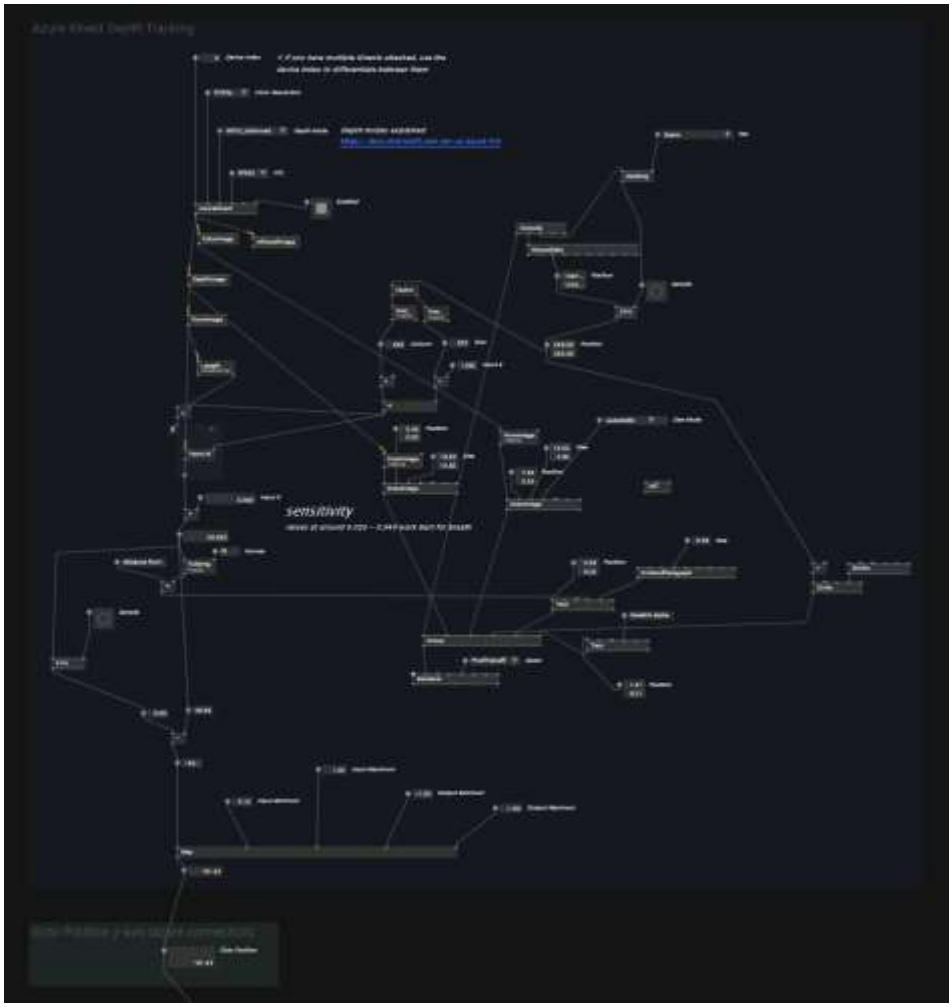

Figure 7 Azure Kinect Depth Training

Figure 8 is an image of the Damper in VVVV that manages the balloons movement in order for it to be smooth and controlled. Minimal measuring errors of the depth sensor can occur. The damper system also helps alleviate this.

Figure 8 Damper

In the 3D Model node tree (Figure 9) a model can be loaded into vvvv. In the case of this prototype, a hot air balloon.

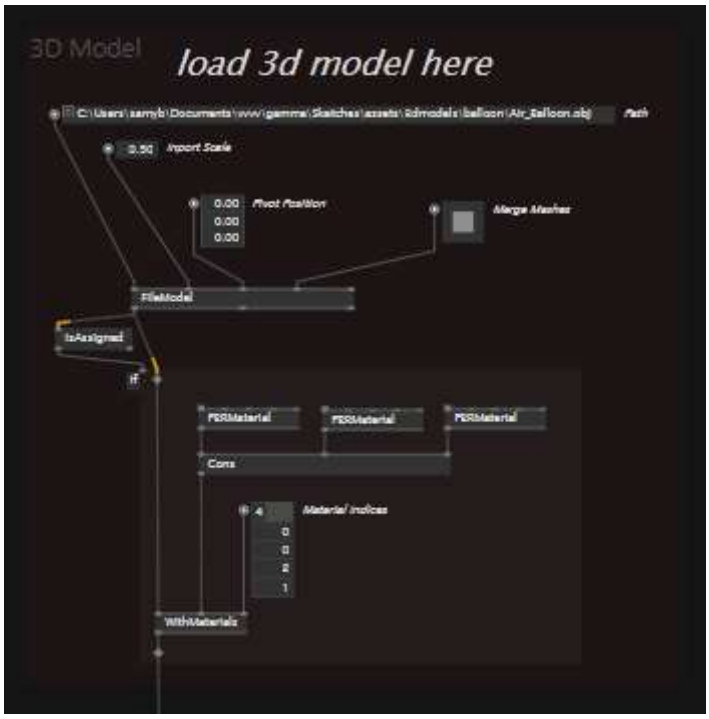

Figure 9 Audio

The audio signal configuration is shown in figure 10.

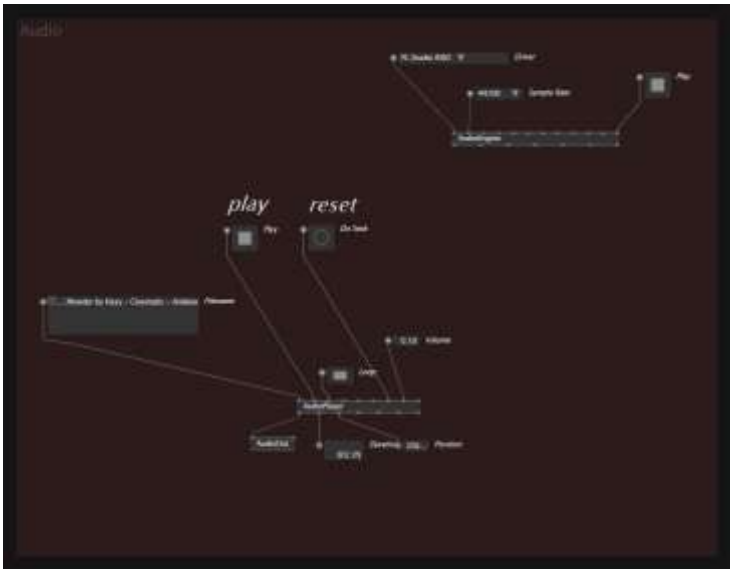

Figure 10 Audio signal configuration

4 BreathX – Defining a user journey

The prototype was designed under the consideration of the user centered design approach: Relating to the project, a concrete user-description was conducted to define the scope of application and target group. Also, an individual user-journey was created.

4.1 Persona

Name: Gudrun Huber
Age: 65

- Divorced, was married for 23 years
- No children, despite intensive hormone therapies
- Introvert
- Pensioner, former nurse (incl. regular night work)
- Overweight, smoker, depression, anxiety symptoms
- No sports for a long time
- She had her first menstrual period quite early but also a late onset of her menopause.
- Tech-savvy: she has her own smartphone and keeps in contact via WhatsApp
- Her mother died of breast cancer.
- Annual preventive examination for mammography because of her family background.
- Due to her mother's breast cancer, she is very attentive and regularly goes for a check-up.

<u>Gudruns story:</u>

Gudrung was born on the 4th of April in 1955. She grew up in Vienna where she went to nurse's training school, she completed her degree in 1972 and immediately started working at the AKH in Vienna. She met her ex-husband Anton at the age of 19 and married him when she was 23 years old. Her wish to have children stayed unfulfilled although she and Anton tried for many years and even tried hormone-therapies.
Gudrun and her husband, who refused to adopt a child grew apart more and more. They talked less and fought more and more. Finally, Anton had an affair that led to their divorce after 23 years of marriage.
Not having children and being divorced resulted in Gudrung withdrawing herself from life more and more. With her friends and remaining relatives - she has good contact to her sister and a few old school girlfriends - she hardly discusses private or intimate things with anyone.

She does not want to burden her loved ones with her disease and therefore does not show or tell anyone in what bad place she really is. On the other side she is always there for everybody who needs her and is a very good listener.
A couple years ago she moved from Vienna to Bad Vöslau in a small townhouse with a little garden near the train station. She started working at the hospital in Wr.Neustadt (insurance: OGK) on the ward for internal medicine. Gudrun never learned how to drive a car, so she went back and forth from work by train until she went into retirement at the age of 60.
Due to the fact, that her mother died of breast cancer at a very young age, Gudrun has always been very alert and undertakes preventive med-check-ups, regularly visits her gynecologist.
Her mother's death still weighs Gudrun down. She always feared to get breast cancer herself, so of course she took the invitation of the Österreichische Brustkrebs-Früherkennungsprogramm to undergo a mammography. Because of her family history she is invited yearly instead of every second year. Shortly after receiving the invitation letter, Gudrun scheduled an appointment for a mammography in a nearby radiology-institute. She immediately got her results and as they were suspicious, she had a biopsy, MRT and bone-scintigraphy as well as a blood test (receptor status) shortly after that. Gudrun was diagnosed with an invasive-ductal mamma-carcinoma (IDC). Although being shocked when her life-long fear came true, Gudrun faltered for a few days before she decided to get a proper treatment. Her doctors urged her to start with chemotherapy as soon as possible, so Gudrun did so two weeks after being diagnosed. Two months after her diagnosis the tumor was removed in a surgery. Five weeks after the successful surgery, her wounds are healing well. Gudrun received her last chemotherapy two weeks ago and is ready to start undergoing radiotherapy according to her oncologist. Additionally, she is receiving an adjuvant hormone-therapy as she suffers from a hormone-receptor-positive form of breast cancer. Since being diagnosed Gudrun visits a psychotherapist, who gave her a folder for a self-help group, that Gudrun is still unsure whether to attain or not. Acting on her doctors' advice, Gudrun started autogenic-training and meditating. Mona, who she knows from her stay in the hospital, advised her to do yoga and go walking for a few times per week. She also told Gudrun about radiotherapy, as she herself had to do it before (she was in hospital for her second breast- cancer operation). The two of them sill hold contact.
Gudrun also bought herself a smartphone three years ago to stay in contact with her sister and some friends from school via WhatsApp. In her leisure time Gudrun likes to paint, works in her garden or cuddles with her cat Milo. She likes visiting art galleries for inspiration. Gudrun sells her paintings on handicraft-markets.

4.2 Anti-Persona

Name: Anna-Maria Angerer
Age: 85

- Widowed
- Two children
- Factory worker, working in shifts including night shifts
- Smoker
- No TV, no smartphone
- Unathletic, not interested in sports
- Overweight
- Suffering from recurring breast cancer
- Underwent several radiotherapies, no problems concerning DIBH
- Received several chemotherapies
- Underwent two surgeries
- Sceptical concerning technology and innovation
- Stressed by changes
- Not interested in trying out or learning new things

4.3 User Journey

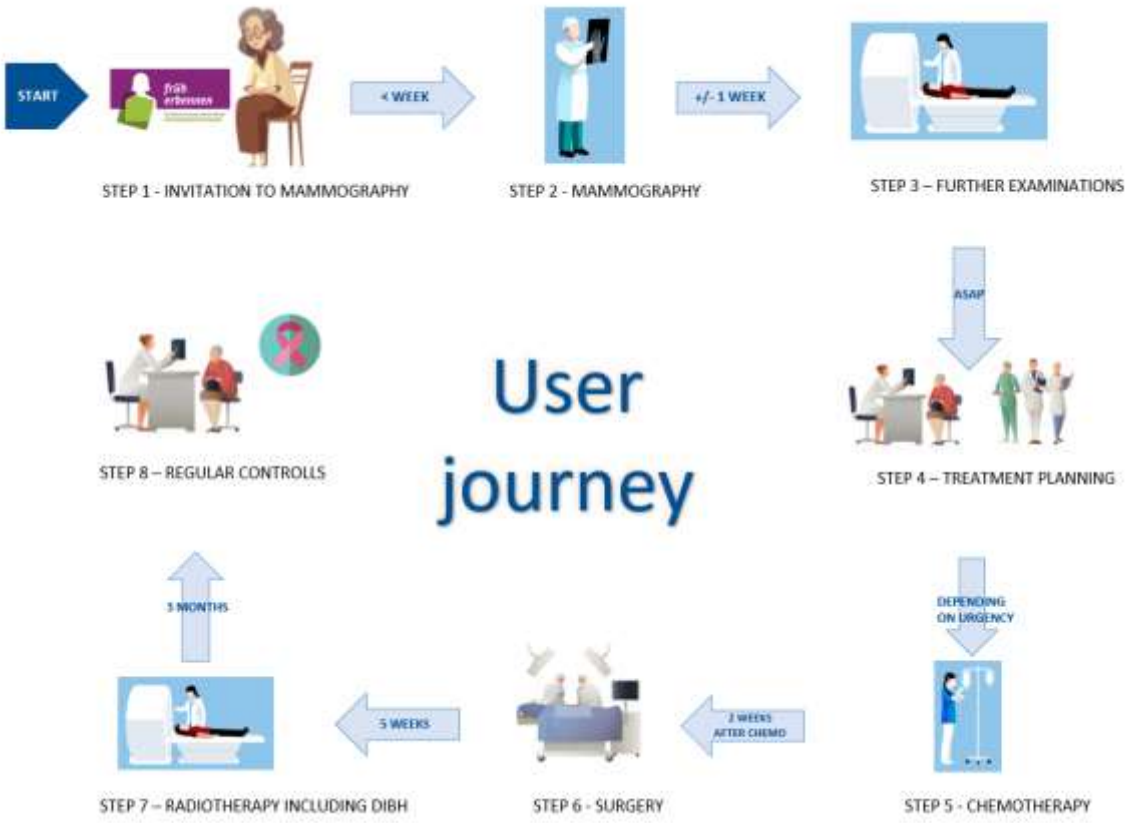

Table 1 User Journey - Steps

STEP 1 – INVITATION TO MAMMOGRAPHY

Every second year, starting from the age of 45, austrian women get invited to mammography (https://www.frueh-erkennen.at/ueber).

STEP 2 – MAMMOGRAPHY

If the radiologist detects a suspicious lesion in the mammography, the patient is sent to the hospital for further examinations.

STEP 3 – FURTHER EXAMINATIONS

A punch biopsy is performed in the hospital. If degenerated or malignant cells are detected, further examinations such as an MRT, a bone scintigraphy, CT and a PET-CT are performed, to come to an exact diagnosis.

STEP 4 – TREATMENT PLANNING

After diagnosis, the patient is informed about their therapeutic possibilities. Based on the patients' medical record, a team of qualified doctors and psychologists discusses and

plans an individual treatment for every patient.

STEP 5 – CHEMOTHERAPY

Many patients receive chemotherapy to reduce tumour-size before surgery.

STEP 6 – SURGERY

Depending on the diagnosis either part of the breast is removed or a complete mastectomy IORT is conducted.

STEP 7 – RADIOTHERAPY INCLUDING DIBH

Left sided breast cancer is treated with percutaneous RTX including DIBH-Technique. A week prior to the RTX a planning CT is performed.

STEP 8 – REGULAR CONTROLLS

Patients are considered tumour-free when no tumour-cells are detected in the PET-CT. To discover possible recurrences, semi-annual PET-CTs are performed.

5 BreathX – The Science behind user engagement in therapy

The aim of this chapter is to summarize the current research status to the following points:

- Effect of music interventions in breast cancer patients (anxiety, stress, depression)
- Auditive and visual feedback to regulate respiration during radiotherapy
- Pranayama-training as preparation for the Deep inspiration breath hold technique (DIBH) during radiotherapy in breast cancer patients
- Breast-Cancer patients emotional experiences during radiotherapy treatment

5.1 Hypothesis

1. Audio visual feedback during radiotherapy improves patient's compliance through stress and anxiety reduction.
2. Audio visual feedback during radiotherapy improves the treatment efficiency of left-sided mama-carcinoma patients.
3. Pranayama training as preparation for radiotherapy-treatments improves DIBH-technique performance in breast cancer patients.

5.2 Methodology

We have conducted a literature search on the databases CINAHL, PubMed, Cochrane Library. Furthermore, we consulted the reference lists of suitable studies and literature reviews. Moreover, we also searched for basic information about radiotherapy treatment, complications, and risk factors as well as epidemiological data of Austria to create a holistic knowledge base.

5.3 Findings/Results

5.3.1 Music interventions

In general, music interventions can reduce the heart rate, respiratory rate, and blood pressure of a patient. It has also been proved that music is an effective way to reduce pain, fatigue, to increase patient's quality of life and to reduce recovery time and duration of hospitalization (de Witte et al., 2020).

Bulfone et al. (2009) have shown, that music interventions have a positive effect on breast cancer patients. Gramaglia et al. (2019) and Rossetti et al. (2017) observed a strong and significant reduction of stress, depression and anxiety through music intervention during radiotherapy. Also de Witte et al. (2020) have come to the same results. Nguyen et al. (2010) have found out, that music intervention also influences the respiration rate through the calming and anxiolytic effect. Greenlee et al. (2017) recommend music therapy, meditation, stress management, and yoga for stress and anxiety reduction in breast cancer patients.

Furthermore, a significant stress relieving, and relaxing effect was reported by using auditory alpha activity training in a range of 8-12 Hz. An increase of ten percent in alpha activity in posterior sites occurs (van Boxtel et al., 2012). Alpha waves (8.1-13 Hz) are produced by the brain during light relaxation and with closed eyes. Music that is subliminal (frequency range 0.1 - 11 Hz) can help to relieve stress and relax (Rosicki, 2015).

5.3.2 Auditive and visual feedback

The implementation of audio and visual feedback significantly reduces the treatment delivery time of respiratory gated radiation therapy (Linthout et al., 2009). Furthermore, personalized audio-visual biofeedback improves the treatment efficiency and ameliorates the dose delivery precision. The respiratory guidance also reduces residual target motions within the gating window by performing the DIBH-technique (He et al., 2016).
Yu et al. (2015) reported, that there is no significant difference between the effectiveness of audio-only and audio-visual biofeedback.

Baba et al. (2016) pointed out, that audio feedback improves the stability of the respiration cycle, but also increases the amplitude of respiratory curves. They also found out, that adding visual feedback to the audio feedback improves the stability of the amplitude and the lowest point of the respiration cycle. Even if the audio-visual feedback is the most effective one to stabilize the respiration, it also needs some kind of individualizing possibilities for each patient (Baba et al., 2016).

5.3.3 Pranayama – Training (Yoga)

Pranayama is a breath regulation practice. It builds a main part of Yoga and means inhaling, exhaling, and holding the breath in a specific kind of sequence. It influences the breathing timing, duration and frequency of every breath and breath hold consciously. Pranayama has many beneficial aspects:

- Decreases stress
- Improves sleep quality
- Increases mindfulness
- Reduces high blood pressure
- Improves lung functions
- Enhances cognitive performance
- Reduces cigarette cravings
- Etc.

(Nunez & Sullivan, 2020)

Regarding the stress reduction effect, Pranayama practice reduces the perceived stress level by stimulating the nervous system. This process beneficially improves the human stress response (Sharma et al., 2013). Breast cancer patients who perform Pranayama along with radiotherapy have a significantly lower worry and anxiety level (Chakrabarty et al., 2016).

Furthermore, the Yoga breathing method induces a higher awareness of the breathing patterns, which causes a better level of emotional regulation and a calming effect. Conscious breathing results in an increased concentration of oxygen, which causes improved focus and concentration (Shastri et al., 2017).

Pranayama, as a type of breathing exercise, strengthens the lungs according to clinical studies. Already one hour of pranayama exercise over a period of about 6 weeks significantly improves several lung function parameters in pneumological tests (Shankarappa et al., 2012).

5.3.4 Breast cancer patients' emotional experiences

In general, 12 – 47% of breast cancer patients report baseline anxiety. 11 – 16% report to suffer from anxiety and depression. In total about 50% of all breast cancer patients experience emotional stress. A quarter of them is affected by clinically significant psychological disorders. Breast cancer patients are confronted with feelings like fear for their health, uncertainty about their health related outcomes and an upcoming loss of control (Mayr et al., 2020).

Patients are confronted with both, psychological and physical challenges. During radiation therapy, anxiety and stress are augmented by the demanding physical performance which is required to perform the DIBH-technique during the procedure. The DIBH-technique calls for physical control and coordination of thoracoabdominal muscles. This is needed to breath in deeply, prolonged and hold the breath stable for a defined amount of time. This kind of breath-technique is not implemented intuitively by the patient. Moreover, breast cancer patients are confronted with a rapid on-demand cooperation, strictly timed within a stressful procedure sequence and within a frantic treatment schedule. There is nearly no time to prepare. All these factors create an overstraining situation and influence patients coping strategies (Mayr et al., 2020).

Anxiety and stress are closely coupled with shallower and faster breathing patterns, creating a vicious cycle that impacts the optimal breath-holding performance. These stressors that occur can make the performance of DIBH- technique difficult for the patient and affect both, the therapy success and radiation exposure of the surrounding tissue as well as the efficiency of the therapy (Mayr et al., 2020).

6 Outlook

We only tested out prototype in a non-clinical setting. In a next step the prototype could be tested in a clinical setting connecting it to the existing infrared camera in the treatment room. Furthermore, a cell phone app could be planned to prepare patients for radiation therapy. Patients could use it to train their breathing with various exercises.

Figures

Tables

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