

# Survey on Deep Inspiration Breath-holding in the Netherlands

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GRADUATION REPORT

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## Preface

This is the graduation report 'Survey on Deep Inspiration Breath-holding in the Netherlands'. This report was written as part of my graduation from MBRT at Inholland University Haarlem.

I would like to thank my supervisors Michael Parkes, senior scientific researcher breathing control strategies and Irma van Dijk, senior scientific researcher radiotherapy from the Amsterdam UMC, location AMC, for guidance and support during this research. I would also like to thank Martijn Kamphuis, teacher physics at Inholland University, for the personal guidance in writing this graduation report. Last, I would like to thank all respondents for answering the survey. Due to the cooperation, I was able to conduct the research and to write this graduation report.

Femke Sikkink  
Lutjebroek, 29-05-2022

# Summary

## Introduction

Deep Inspiration Breath-Holding (DIBH) is widely used to control respiratory motion, especially in radiotherapy of left-sided breast cancer. Patients perform breath-holds after inhaling room air (21% oxygen). Some patients cannot hold their breath for this long and they will be treated during free breathing which increases the risk of late cardiac toxicities. Several studies showed that replacing room air by 60%O<sub>2</sub> can double the breath-hold duration. There is no formal information on how long patients at Dutch radiotherapy departments are asked to hold their breath, and by which technique. It is also not clear how often patients are treated during free breathing. The following main question has been formulated:

*'What are the main considerations and what kind of issues are encountered when using DIBH in clinical practice in the Netherlands when patients with left-sided breast cancer are treated with DIBH?'*

## Methods

To investigate this, a survey has been sent to all 22 radiotherapy departments in the Netherlands. Per department, one radiation therapist (RTT), one radiation oncologist and one medical physicist were asked to complete the survey. 46 of the 66 respondents completed the survey. The answers within a department are compared with each other.

## Results and discussion

The results have shown that a lot of different techniques are used in radiotherapy departments in the Netherlands. The majority of the departments (70%) uses the same breath-hold method for all patients, while the main reason that patients are treated during free breathing is that they cannot hold their breath long enough (75%).

## Conclusion

Voluntary breath-hold is the mostly used method using 8 breath-holds of 25 seconds. The respondents do recognize the benefits of using 60%O<sub>2</sub>, but they are not sure about using it in clinical practice. The percentage of patients who cannot hold their breath for the required duration is 5%, with the most common reason that patients cannot hold their breath long enough.

**Contents**

Preface .....2

Summary .....3

*Introduction*.....3

*Methods* .....3

*Results and discussion*.....3

*Conclusion*.....3

1. Introduction .....6

    1.1 *Cause* .....6

    1.2 *Problem* .....7

    1.3 *Aim and relevance* .....7

    1.4 *Questions* .....8

2. Methods.....9

    2.1 *Type of research and design* .....9

    2.2 *Research settings*.....9

    2.3 *Research population/research object*.....9

    2.4 *Time period*.....9

    2.5 *Procedure*.....9

    2.6 *Variables and measurement instruments* ..... 10

    2.7 *Data analysis* ..... 10

*Secondary research question 1* ..... 11

*Secondary research question 2*..... 11

*Secondary research question 3*..... 11

*Main research question* ..... 11

3. Results ..... 12

    3.1 *Respondents*..... 12

    3.2 *Secondary research questions* ..... 12

*Secondary research question 1* ..... 12

*Secondary research question 2*..... 14

*Secondary research question 3*..... 15

4. Discussion ..... 18

    4.1 *Interpretation results* ..... 18

    4.2 *Comparison literature* ..... 19

    4.3 *Strengths and limitations*..... 20

    4.4 *Generalizability* ..... 20

5. Conclusion ..... 21

5.1 Secondary research question 1 .....	21
5.2 Secondary research question 2 .....	21
5.3 Secondary research question 3 .....	21
5.4 Main research question .....	21
6. Recommendations .....	22
References .....	23
Attachments .....	25
<i>Attachment 1: Information sheet and survey</i> .....	25
<i>Attachment 2: Results of the remaining questions</i> .....	30

# 1. Introduction

## 1.1 Cause

In 2018, 17 million people worldwide were diagnosed with cancer.(1) In more than half of the patients diagnosed with cancer, radiotherapy is a part of the treatment or the only one performed.(2)

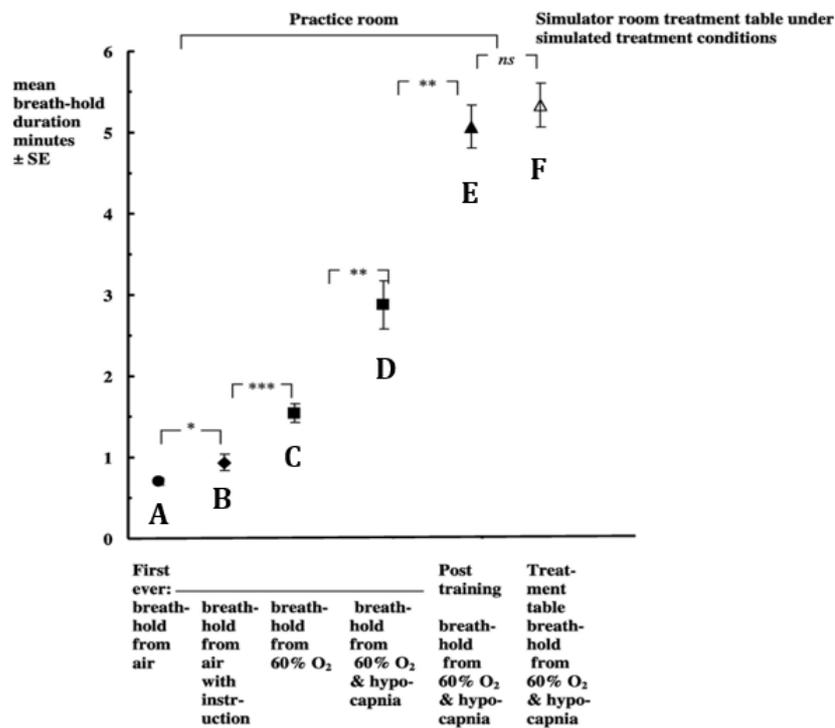
Radiotherapy needs to be as accurate as possible, because the tumor must be given a high dose, while the organs at risks (OARs) must be spared as much as possible to minimize the risk of acute and chronic side effects.(3) Although the tumor can be accurately located, treating tumors in the thoracic and upper abdomen is challenging because respiratory motion causes a variable tumor position.(4) Respiratory control strategies as breath-holding and compression of the abdomen were introduced to reduce the variation in tumor position. Once the variation is reduced the treatment margins can be narrowed leading to a lower dose to OARs while the high dose in the tumor does not change.(4)

Deep Inspiration Breath-Holding (DIBH) is widely used to control respiratory motion, especially in radiotherapy of left-sided breast cancer.(5) During such a radiotherapy treatment fraction patients perform multiple short breath-holds after inhaling room air (21% oxygen;  $O_2$ ).(6) Several studies have shown the improvements offered by DIBH compared to free breathing, such as radiation dose reduction to the heart, since the distance from the heart to the chest wall is enlarged because of a consistently greater lung volume.(6–8) The risk of late cardiac toxicities will be reduced, because the heart will be less exposed to radiation.(6–8) Multiple breath-holds of 20-30s are used in each treatment fraction, but some patients, for various undefined reasons, cannot hold their breath for this long.(9) They are currently treated without breath-holding (i.e. under free breathing), but would benefit from the heart sparing effects of breath-holding if they could be helped to hold their breath longer.(9)

In clinical practice, radiotherapy may be very stressful for many patients. This can complicate the breath-hold treatment, because they will reach the break-point earlier.(10) The break-point is the moment that patients start breathing again because they cannot hold their breath any longer.(11) Breath-holding is a voluntary act but the breakpoint is involuntary and almost impossible to control. There are different views on the breakpoint and the precise mechanism of the breakpoint is not known.(11) Parkes et al. showed that breath-hold duration is prolonged (the breakpoint is delayed) by training (good technique of maximum inhalation and repeating this), and by breathing 60% $O_2$  instead of room air before the start of the breath-hold.(11)

Another study of Parkes et al. showed that without any preparation, people can hold their breath for  $54 \pm 6$ s (mean  $\pm$  standard deviation SD) after instruction for a DIBH with room air.(12) After training, the breath-hold duration with room air increased to  $96 \pm 6$ s.(12) This was improved by replacing room air by 60% $O_2$  before breath-holding. The mean breath-hold duration increased to  $150 \pm 12$ s (Figure 1A, B, C).(12) When training was combined with the use of 60% $O_2$  and hypocapnia induced by non-invasive mechanical ventilation, the mean breath-hold duration over all participants was  $372 \pm 18$ s (Figure 1D, E, F).(9,11,12) Breath-holding causes the systolic blood-pressure to increase, so this technique is not completely riskless, but the rising pressure is acceptable and easily monitored.(9,12) Of these prolongation techniques, preparation with 60% $O_2$  without the use of a mechanical ventilator

is an easy method to apply, because this involves no sophisticated equipment.(12)



**Figure 1:** First ever breath-hold durations (A) in 15 breast cancer patients significantly improve after instruction (B) and after breathing 60% O<sub>2</sub> (C) instead of room air. D, E and F show increased breath-hold durations after non-invasive mechanical ventilation with 60% O<sub>2</sub> and hypocapnia (Figure adapted from (11)).

The use of 60%O<sub>2</sub> does not affect the systolic blood pressure.(9,12) Using 60%O<sub>2</sub> is an easy, safe, inexpensive and universally applicable method which enables patients who cannot breath-hold for longer than 20-30s with room air, to hold their breath for more than twice as long.(9,12)

### 1.2 Problem

In clinical practice in the Netherlands, patients with left-sided breast cancer are asked to hold their breath for around 20 to 30 seconds using only room air, but there is no formal information on exactly how long patients at Dutch radiotherapy departments are asked to hold their breath, and by which technique. It is also not clear how many patients cannot hold their breath for 20 to 30 seconds. If patients are then treated during free breathing, the risk of cardiac toxicities may be increased, which can be disadvantageous for patients.

### 1.3 Aim and relevance

The clinical practice of DIBH will be collected through a survey (Attachment 1). This is about patients with left-sided breast cancer who are treated with radiotherapy in the Netherlands. The aim of the study is to identify the main considerations and the issues encountered using DIBH. The aim of this survey is two folded. For the patients who can be treated with DIBH, it would be useful to know e.g., what kind of breath-hold instructions they receive, for how long they are asked to hold their breath, how many breath-holds a session consists of or whether a treatment machine turns off once chest inflation is below a measured level. Patients who cannot hold their breath for the required 20 to 30 seconds might benefit from the use of 60%O<sub>2</sub>. They are currently treated during free breathing and might benefit from the heart sparing benefits.

The survey will also provide the opportunity to inform all radiotherapy departments about the benefits of using 60%O<sub>2</sub>, by means of an information sheet the respondents will receive. Increasing the awareness of the benefits of using 60%O<sub>2</sub> instead of room air, could lead to more colleagues in the Netherlands considering the adoption of 60%O<sub>2</sub> to improve breath-hold durations in some or many of their patients. The survey will also give an indication if people in the field are willing to use 60%O<sub>2</sub> in the future.

The clinical gains from offering 60%O<sub>2</sub> to all patients to enable them performing longer breath-holds include the advantage of requiring fewer breath-holds per fraction. This would also be less tiring for patients and would increase their confidence. Furthermore, if all patients could hold their breath for a longer time, the smaller number of breath-holds per fraction could mean that more patients could be treated each day, which will lead to greater efficiency in clinical practice. Finally, sharing the results of the survey with the participating departments can stimulate them to improve their protocols when they see that other departments have better results.

## 1.4 Questions

To get more insight into the clinical practice of DIBH by left-sided breast cancer in radiotherapy in the Netherlands, the survey should answer the main research question and the three secondary research questions:

- What are the main considerations<sup>1</sup> and what kind of issues<sup>2</sup> are encountered when using DIBH in clinical practice in the Netherlands when patients with left-sided breast cancer are treated with DIBH?
  - How long are patients asked to hold their breath with how many breath-holds and which method is used in clinical practice in the Netherlands when patients with left-sided breast cancer are treated with DIBH?
  - What percentage of patients with left-sided breast cancer who should be treated with DIBH during radiotherapy in the Netherlands, cannot perform DIBH and for what reasons?
  - To what extent are radiation therapists (RTTs), radiation oncologists and physicists willing to use 60%O<sub>2</sub> to enable patients who cannot breath-hold for 20-30s to hold their breath for the required duration?

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<sup>1</sup> Main considerations involved: The breath-hold duration, the number of breath-holds, the method which is used and the view on the use of 60%O<sub>2</sub>.

<sup>2</sup> Issues involved: The percentage of patients who cannot breath-hold for the required duration and for what reasons.

## **2. Methods**

### **2.1 Type of research and design**

The variables of this study are collected with the use of a survey (Attachment 1). This thesis is part of a larger research project, so the survey contains more questions and not all of them have been analyzed within this thesis. This study is mostly quantitative in design, since mainly multiple choice questions are being used and data from many different departments must be presented in a clear manner.(13) In numbers and percentages is expressed how many respondents give a certain answer e.g. how many answered with 'yes' and how many said 'no'.

The survey contains one question with a qualitative aspect that has been discussed in this thesis (Attachment 1, question 21). An open question is used to collect the opinion of the respondents and not to influence their answers by means of a multiple choice option. The other questions are multiple choice, and the survey contains two questions where the respondent had to estimate or look up a number of patients. The survey has been conducted at one certain moment, which means that all variables are measured at the same time. This makes it a cross-sectional study.(14)

### **2.2 Research settings**

The initiating department is the department of radiotherapy at location AMC of the Amsterdam UMC. The Amsterdam UMC has only been in existence since 2018, since the AMC and the VUmc started merging. Annually, 56000 patients are admitted only at the location AMC.(15) The department of radiotherapy yearly treats about 160 patients with left-sided breast cancer.(16)

### **2.3 Research population/research object**

The survey focuses on radiotherapy departments who are treating patients with left-sided breast cancer. It has been sent to all 20 main departments and the three proton centers in the Netherlands. Proton centers are also included, because their techniques might differ. From each department, one RTT, one radiation oncologist and one physicist, involved in breast cancer treatment, were asked to complete the survey. Some of the radiotherapy departments have 'satellite' departments, which were not invited to complete the survey, because they most likely use the same protocols as the main location. An exception applies to the Amsterdam UMC, which consists of the AMC and the VUmc. This merger is still an ongoing process and both hospitals are currently using their own protocols.

### **2.4 Time period**

The research proposal was approved on September 13, 2021, by the research group of 'Hogeschool Inholland'. From this moment, the research has been carried out, i.e. preparing the survey questions. The surveys has been sent out in the middle of February. After this, results have been analyzed and the final report will be submitted before May 29, 2022.

### **2.5 Procedure**

To define the relevant participants (staff involved in left-sided breast cancer treatment), contact details of the participants were collected by making use of acquaintances in the departments. Before the survey was completed, an information sheet was sent with some background information and some information about the goal of this study (Attachment 1). The survey has been set up and sent in 'Google Forms'.(17)

We (and the Google Forms software) estimated that the survey will take approximately 15 minutes to complete. We thought it is reasonable to allow 10 working days for each participant to return the survey. If responses were not received within that time, a reminder email has been sent with the request to respond within a further week.

## **2.6 Variables and measurement instruments**

The Google Forms software is used to issue the survey questions. The variables are the answers given by the participants. The three measurement levels 'nominal', 'ordinal' and 'continuous' are all used in the survey (Attachment 1). The study considers two dependent variables: 1. Main considerations involved: the breath-hold duration, the number of breath-holds, the method which is used and the view on the use of 60%O<sub>2</sub>. 2. Issues involved: the percentage of patients who cannot breath-hold for the required duration and for what reasons. The independent variables are the answers to some more general background questions which are an important part of the survey e.g., the department where the respondents are working, how long have they been working there and their role in the department.

The survey consists of 28 questions and is developed specifically for this research, since no validated surveys are available on this specific topic. The survey starts with some general questions followed by the most important part with the substantive questions about the use of breath-holding in the department of the respondent. At the end, the respondents were asked if they would like to receive the results. Most questions are multiple choice. This enabled participants to answer the questions with minimal time investment.

To increase reliability, three respondents per department were asked to complete the survey, and the average answer was calculated. Each profession has their own area of specialization. The respondents had to look up an exact number of patients or, when this was not possible, estimate a number of patients. For this, it was useful when a breast radiation oncologist completed the survey. They can make an experience-based estimation because they are involved by all the breast cancer patients.

To maximize the validity of the survey, experts in the field were consulted.<sup>(14)</sup> The survey was first tested in Amsterdam UMC. Several RTTs were asked to study the survey carefully with the knowledge they have from practice and to provide feedback. In doing so, they paid attention to the completeness of the answer categories and whether other questions should be asked or whether a question was superfluous. The feedback has been processed in the survey. For example, for question 13 it was not clear whether it concerned the number of breath-holds for a complete radiation session including the imaging or only the radiation. This has been edited to make it clearer.

## **2.7 Data analysis**

The analysis of this research is based on descriptive statistics.<sup>(14)</sup> The answers to the survey questions have been analyzed in Excel (Office 365, version 2110). To solve any ambiguities, (for example, because respondents within a department gave different answers to a question), the respondents have been telephoned to resolve the ambiguity.

The general questions are used to get an overview of the respondents who completed the survey. A pie chart and a histogram have been created. Below, the analysis of the survey will be discussed for every secondary research question separately, followed by the analysis of the main research question.

### ***Secondary research question 1***

The survey questions 4, 10 to 13 and 20 to 25 belong to the first dependent variable: the main considerations. Question 4 and 10 to 13 will also give an answer to the first secondary research question. These questions have been answered using nominal and ordinal answer categories. The answers are presented using numbers and percentages of occurrence for each answer and histograms have been made. The average breath-hold duration as used in the Netherlands is calculated.

### ***Secondary research question 2***

The issues encountered have been collected using survey question 14 to 16. These questions also give an answer to secondary research question 2 and have been answered using the answers on a continuous and a nominal measurement level. First, everyone was asked to note the number of patients with left-sided breast cancer they irradiate with breath-holding per year. Then the question was asked how many patients they treat during free breathing because they cannot hold the breath-hold for the required duration. The total number of patients and the percentage of patients irradiated during free breathing instead of breath-hold is calculated. The main reason why patients are treated during free breathing because they cannot hold the breath-hold was also asked in the survey and have been presented in a pie chart.(13)

### ***Secondary research question 3***

Survey question 20 to 25 give an answer to secondary research question 3. The results of question 20 and 22 to 25 have been displayed in histogram which shows the numbers and/or percentages of each answer. The open question about the difficulties have been presented on a qualitative basis. The answers given by the respondents are listed with the occurrence per profession behind them.

### ***Main research question***

After the secondary research questions have been answered, the main research question has been answered. The main considerations are determined by the answer that occurred the most. The percentage of patients who cannot breath-hold for the required duration is calculated in the elaboration of the second secondary research question. The main reason for this is the reason mentioned the most in survey question 16.

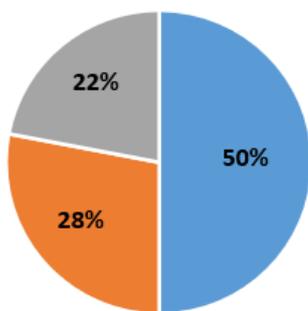
Furthermore, the survey consists of 11 more questions to gain an even better insight into the use of breath-hold. These questions are part of the bigger research project, and the results do not directly apply to the main research question and the secondary research questions asked in this thesis. The results of these questions can be found in Attachment 2.

### 3. Results

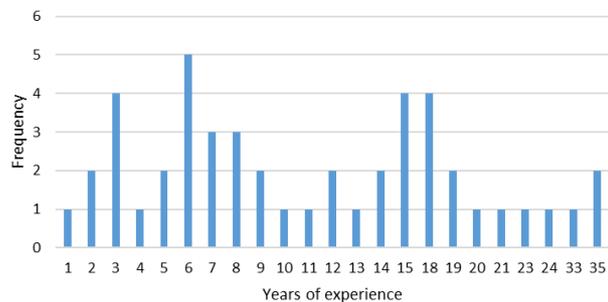
In this chapter the results of the survey are shown using tables and graphs. It is sub-divided in order of the questions in the survey.

#### 3.1 Respondents

The response rate varied from more than 100% in the RTT group (23/22 responses; in one department two RTTs responded) to 59% (13/22) among radiation oncologists and 45% (10/22) among medical physicists. In five departments, all three professions completed the survey. In 13 departments, two of the professions completed the survey and in four departments, only one profession responded. Figure 2 shows the representation per profession as a percentage of all respondents who responded (46/66). Figure 3 shows the distribution of the number of years that respondents are working in their department. It shows that the years of working in a department differs from 1 to 35 years with a median of 10 years.



**Figure 2:** Results of survey question 3. The representation per profession as a percentage of all respondents who responded (46). Blue = RTTs; Orange = Radiation oncologists; Grey = Medical physicists.



**Figure 3:** Results of survey question 2. The number of years that respondents are working in their department. Mean = 12 years, mode = 6 years and median = 10 years.

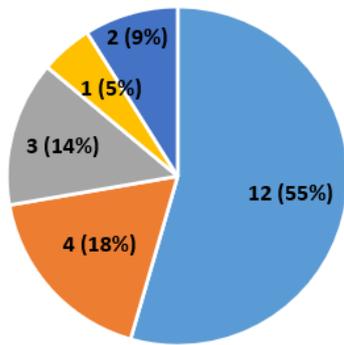
#### 3.2 Secondary research questions

In the next section, the results of the survey questions to answer every secondary research question are presented separately. The answers to the other 11 survey questions (6-9, 11, 12, 17-19, 26 and 27), which do not directly apply to the main research question and the secondary research questions of this report can be found in Attachment 2.

##### Secondary research question 1

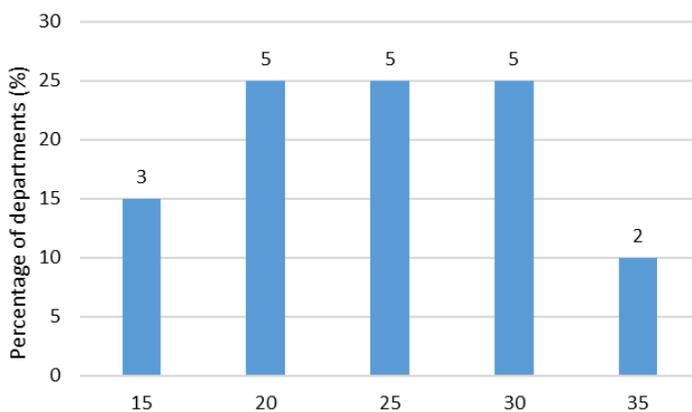
To answer the first secondary research question 'How long are patients asked to hold their breath with how many breath-holds and which method is used in clinical practice in the Netherlands when patients with left-sided breast cancer are treated with DIBH?', the survey questions 4 and 10 to 13 have been analyzed.

The majority of the departments (20/22; 91%) uses some form of breathing management for left-sided breast cancer treatment (Figure 4). This management is predominantly voluntary breath-holding, where the breath-hold is visually checked with a light field or by laser alignment with on the skin a reference mark (12/22; 55%). This is followed by active breathing control (4/22; 18%), where a spirometer is used to monitor the airflow throughout the respiratory cycle. One department uses a combination of voluntary breath-hold and real-time position management using an infrared camera and real time coaching. None of the proton centers uses breath-hold.



**Figure 4:** Results of survey question 4: The breath-hold technique used in the 22 departments. Light blue = Voluntary breath-hold; Orange = Active breathing control; Grey = Real-time position management; Yellow = Combination of voluntary breath-hold and real-time position management; Dark blue = Breath-hold is not used.

Next, the 20 departments that indicated to use DIBH for left-sided breast cancer treatment answered the question on what minimum breath-hold duration is required from patients. Figure 5 shows the distribution of the requested minimum breath-hold durations with a range from 15 to 35s and a median of 25s.

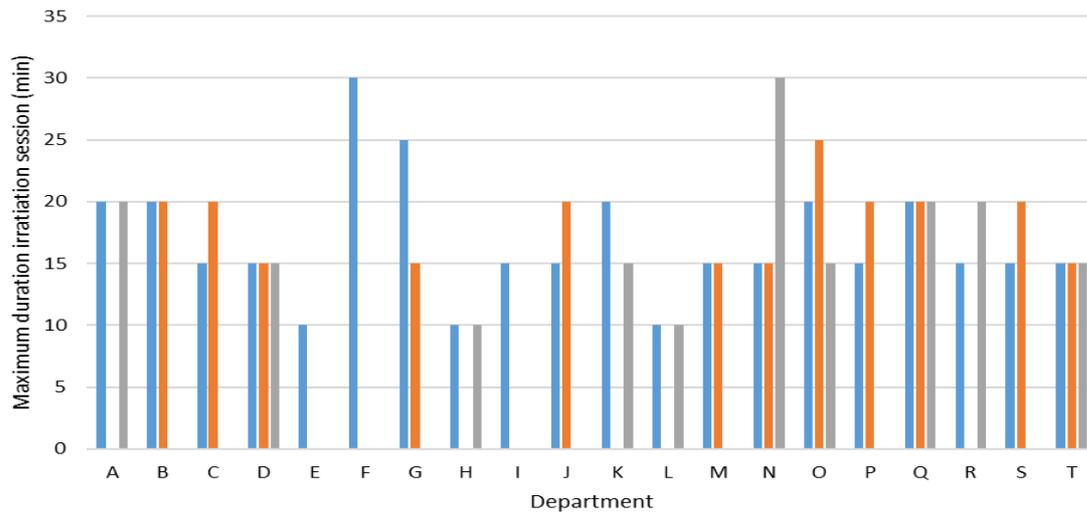


**Figure 5:** Results of survey question 10. Minimum breath-hold durations in the departments (s).

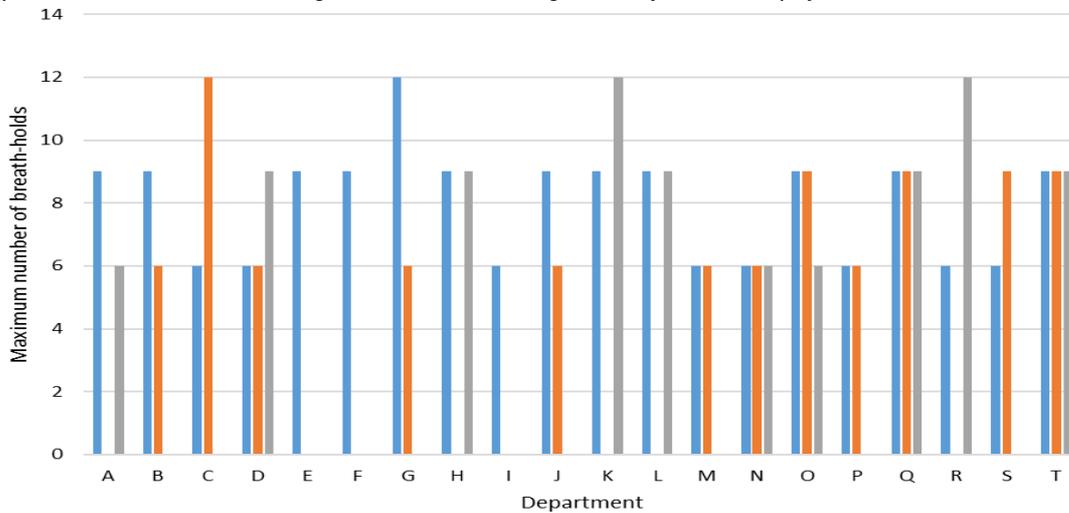
Survey question 11 asked whether the same required DIBH duration is maintained for all patients. The majority of the departments (14/20; 70%) do require the same breath-hold duration from all patients, whereas 6 out of 20 departments (30%) adapt the breath-hold duration to the patients ability.

The treatment session durations as reported by every profession in each of the departments (A-T) are displayed in figure 6A. The figure shows the maximum duration of a treatment session with multiple DIBH. This duration is defined as from the moment the patient is positioned on the table until the moment the patient gets off the table. The answers vary from 10 to 30 minutes with an overall mean of 17 minutes (mode and median are both 15 minutes).

Similarly, figure 6B shows the number of breath-holds as reported per profession in every department, varying from 6 to 12 breath-holds with a mean of 8 (mode and median are both 9).



**Figure 6A:** Results of survey question 12. The maximum irradiation session time per profession in each department. Blue = RTTs; Orange = Radiation oncologists; Grey = Medical physicists.

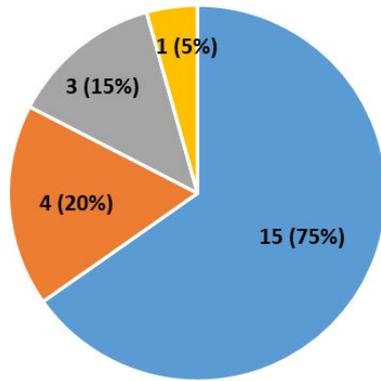


**Figure 6B:** Results of survey question 13. The maximum number of breath-holds per irradiation session per profession in each department. Blue = RTTs; Orange = Radiation oncologists; Grey = Medical physicists.

### Secondary research question 2

To answer the secondary research question ‘What percentage of patients with left-sided breast cancer who should be treated with DIBH during radiotherapy in the Netherlands, cannot perform DIBH and for what reasons?’, survey questions 14 to 16 have been analyzed.

Twenty departments use a breath-holding method for the treatment of patients with left-sided breast cancer. It was unknown how many patients are treated during free breathing instead of breath-holding. In survey question 14 and 15, the respondents were asked to look up or estimate the number of patients with left-sided breast cancer treated in their department, and the number of patients with left-sided breast cancer treated during free breathing. These questions were answered by 15/20 photon departments, who reported to treat 4263 patients in total. In these departments a total of 217 patients (5%) were treated during free breathing. The most common reason for that is because patients cannot hold their breath long enough (15/20; 75%). The second reason is because patients cannot follow the instructions (4/20; 20%) (Figure 7).

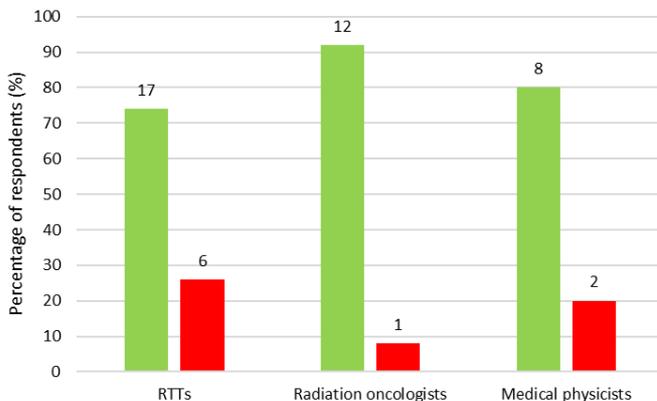


**Figure 7:** Results of survey question 16. The most common reason patients are treated with free breathing. By this question, more answers were possible, so the percentages do not add up to 100%. Blue = Patients cannot hold their breath long enough; Orange = Patients cannot follow the instructions; Grey = Patients cannot hold their breath at a constant inflation volume, which makes the breath-hold inconsistent; Yellow = The heart dose does not matter because of patient's age.

### Secondary research question 3

Survey questions 20 to 25 have been analyzed to give an answer to the third secondary research question 'To what extent are RTTs, radiation oncologists and physicists willing to use 60%O<sub>2</sub> to enable patients who cannot breath-hold for 20-30s to hold their breath for the required duration?'

Figure 8 shows that the vast majority of respondents (74% of the RTTs; 92% of the radiation oncologists and 80% of the medical physicists) recognized the advantages of doubling breath-hold duration by using 60%O<sub>2</sub>.



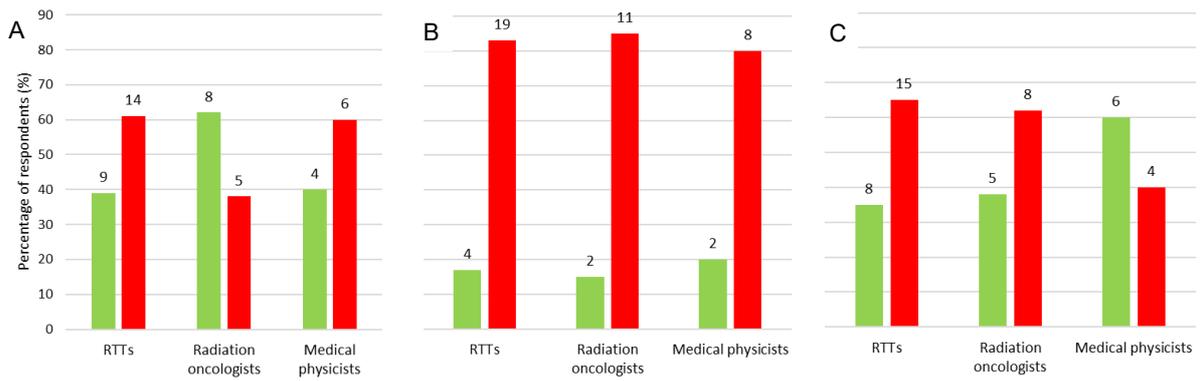
**Figure 8:** Results of survey question 20. Whether or not a respondent sees any clinical advantages in doubling breath-hold duration with 60%O<sub>2</sub>. Green = Yes; Red = No.

Next, the respondents were asked if they would expect any difficulties in using 60%O<sub>2</sub> to double breath-hold duration (Table 1). The most given answer is that no difficulties are seen (30% of the RTTs, 23% of the radiation oncologists and 40% of the medical physicists). The impact for patients and the higher workload are the second most mentioned difficulties. Some radiation oncologists also consider about the waste of material. The least mentioned difficulty is the absence of scientific proof.

**Table 1:** The answers given to survey question 21: Expected difficulties in using 60%O<sub>2</sub> to double breath-hold duration as indicated per profession.

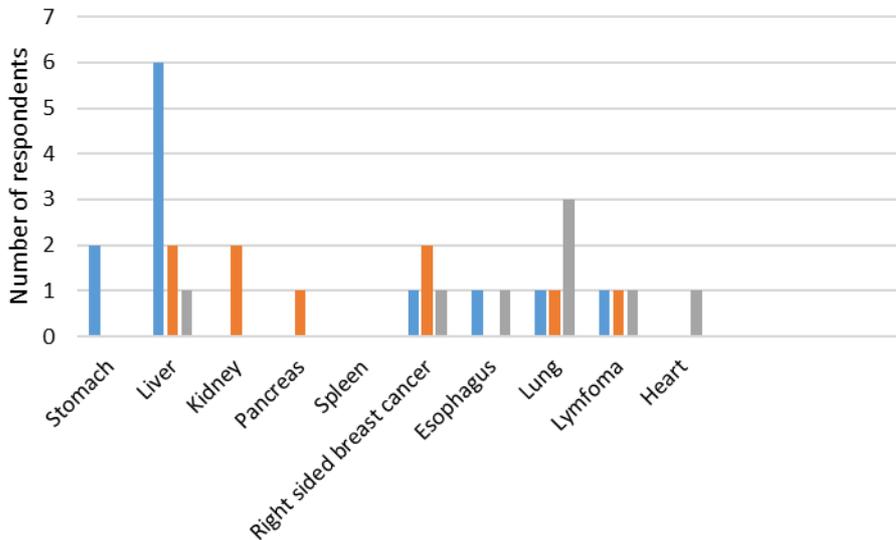
	RTTs N=23	Radiation oncologists N=13	Medical physicists N=10
	N (%)	N (%)	N (%)
None	7 (30)	3 (23)	4 (40)
Impact for patients	5 (22)	2 (15)	2 (20)
Higher workload	4 (17)	3 (23)	2 (20)
Learning a new workflow	1 (4)	3 (23)	2 (20)
Unclear how it works	3 (13)	- (-)	3 (30)
Expensive	3 (13)	1 (8)	1 (10)
Not all treatment rooms are equipped with an oxygen supply	1 (4)	3 (23)	1 (10)
Costs time	2 (9)	1 (8)	- (-)
More waste of material	- (-)	3 (23)	- (-)
Little time gain	2 (9)	- (-)	- (-)
Absence of scientific proof	- (-)	1 (8)	1 (10)

The answers given to question 22 to 24 about the interest of using 60%O<sub>2</sub> in the future are presented in figure 9. Figure 9A shows the results of the interest of using 60%O<sub>2</sub> to enable patients with left-sided breast cancer to perform DIBH if they cannot breath-hold for the required duration. The majority of the radiation oncologists (8/13; 62%) is interested. Less than half of the RTTs (9/23; 39%) and the medical physicists (4/10; 40%) is interested to consider the use of 60%O<sub>2</sub> for left-sided breast cancer patients who cannot hold their breath long enough. The interest to use 60%O<sub>2</sub> for all left-sided breast cancer patients is much lower as Figure 9B shows; 15 to 20% of the respondents indicates to be interested in using 60%O<sub>2</sub> for all these patients. Figure 9C shows the interest to consider 60%O<sub>2</sub> for other cancer patients than patients with left-sided breast cancer. Medical physicists are most interested (6/10; 60%) to use 60%O<sub>2</sub> for other patient groups, whereas slightly more than 1/3 of the RTTs (8/23; 35%) and radiation oncologists (5/13; 38%) would consider this.



**Figure 9:** Results of survey question 22 to 24. **9A:** The number of respondents who are interested to consider using 60%O<sub>2</sub> to enable patients with left sided breast cancer to perform DIBH if they cannot breath-hold for the required duration. **9B:** The number of respondents who are interested to consider 60%O<sub>2</sub> for all patients with left-sided breast cancer. **9C:** The number of respondents who are interested to consider using 60%O<sub>2</sub> for other cancer patient groups. Green = Yes; Red = No.

The respondents who indicated to consider using 60%O<sub>2</sub> for other cancers than left-sided breast cancer were asked for which patients they would use 60%O<sub>2</sub> (Figure 10). The most mentioned cancer type by the RTTs is the liver (6/8; 75%). The radiation oncologists mainly mentioned liver, kidney and right-sided breast cancer (for all three 2/5; 40%). The most mentioned type of cancer by the medical physicists is lung cancer (3/6; 50%). None of the respondents indicated to consider the use of 60%O<sub>2</sub> for spleen irradiation.



**Figure 10:** Results of survey question 25. The number of respondents per profession who are interested in using 60%O<sub>2</sub> for other cancers than left-sided breast cancer. More answers were possible, so the percentages do not add up to 100%. Blue = RTTs; Orange = Radiation oncologists; Grey = Medical physicists.

## 4. Discussion

The aim of the study was to identify the main considerations and the issues encountered when using DIBH in clinical practice in the Netherlands. For this purpose, a survey was used, which also gave the opportunity to inform all radiotherapy departments about the benefits of using 60%O<sub>2</sub>. The results show that many different methods and techniques are used in radiotherapy departments in the Netherlands when treating patients with left-sided breast cancer. The opinions of the respondents about using 60%O<sub>2</sub> also differ but its potential is recognized in different clinical situations.

### 4.1 Interpretation results

The response rate to the survey was 100%, i.e. there came a response from all departments, therefore, this is an excellent representation of clinical practice in the Netherlands. However, not all professions in every department responded. The overall response rate over all respondents was 70% (46/66 persons responded). This is still a reasonable high response rate. (18) All RTTs responded, while the response rate was much less among the radiation oncologists and the medical physicists. Some of them responded that they were too busy due to vacation time and/or Covid circumstances.

Figure 3 shows that a complete range from newly qualified to highly experienced employees with a median of 10 years filled out the survey. This is highly representative for an average department, having employees with a lot of working experience and employees with less experience.

It is interesting how some answers from different professions in the same department differ. For example, within a department, the reported maximum duration of a treatment session with multiple DIBH varied by 15 minutes. Here it is assumed that the RTTs' answers are most reliable, as they carry out the treatment and have daily experience with the patients. This also applies to the number of breath-holds per irradiation session. Here, the overall mean is 8 breath-holds. When only the answers of the RTTs are taken, the mean is 8 breath-holds as well, so despite the different answers, the mean remains the same.

The results of this survey show that 5% of the patients is treated during free breathing. The most common reason is that patients cannot hold their breath long enough, but it is remarkable that also 70% of the departments require the same breath-hold time for all patients instead of looking at the options for each patient personally. The 5% of patients from this study is the target population for treating left-sided breast cancer (or other types of cancer) with 60%O<sub>2</sub>.

After understanding the implications of the survey questions and presumably having read the information sheet, the vast majority of respondents (74% of the RTTs; 92% of the radiation oncologists and 80% of the medical physicists) recognized the advantages of doubling breath-hold duration by using 60%O<sub>2</sub>. On the other hand, some respondents might hesitate to use 60%O<sub>2</sub> to prolong DIBH when they have read the information sheet, for example because the information sheet mentions that breath-holding causes the systolic blood-pressure to increase. Even though this has been contradicted by the fact that the rising blood pressure is acceptable and easily monitored and the use of 60%O<sub>2</sub> does not affect the systolic blood pressure. (9,12)

The respondents were asked if they see any difficulties using 60%O<sub>2</sub>. Many of the difficulties mentioned can be refuted. The respondents were only given the information sheet, which may not have been comprehensive enough to explain the benefits of 60%O<sub>2</sub>. The information sheet should also not be too long, because then people would not read it. Perhaps respondents had not been given enough information to answer the questions properly. The

most mentioned difficulty is the impact for patients. Prolonging DIBH with 60%O<sub>2</sub> ensures that less DIBHs per fraction would be needed, which could make the treatment less exhausting for patients.(19)

Other much mentioned difficulties are the higher work load and learning a new work flow. In the Amsterdam UMC, location AMC it has been shown that not more than one training session is needed to teach RTTs how it works to use 60%O<sub>2</sub>. Clear work instructions must be made after which it can be applied to a patient who comes for the CT scan.

Some of the respondents fear that using 60%O<sub>2</sub> will cost RTTs extra preparation time on the treatment machine, and that it will not result in gaining time. Time gain might not be the most important reason to prolong DIBH. Patients who are now treated during free breathing because they cannot hold their breath long enough are at higher risk of late cardiac toxicities, because the heart will be more exposed to radiation. Using 60%O<sub>2</sub> for these patients could be really useful to reduce this risk.(6,7) At this stage it is unclear whether there is time gain. On the one hand longer breath-holds means fewer breath-holds, but it also depends on the preparation time.

For the departments where oxygen is not yet available in the treatment rooms, this can be solved with an one-off cost. After this more patients can be treated with DIBH which can be very beneficial for these patients.

What is striking is that the minority of RTTs would like to use 60%O<sub>2</sub> in the future. Also, many RTTs say that they don't see any difficulties using 60%O<sub>2</sub>. This contradicts each other. Maybe they need some more information before they can really give their opinion.

## **4.2 Comparison literature**

The response rate of the study can be compared with the study of Duma et al. (2017). The aim of Duma et al. (2017) was to investigate the personal beliefs of radiation oncologists regarding heart-saving techniques. A survey was set up for radiotherapy departments in Germany, Austria and Switzerland. The overall response rate of the study was 40%.(20) This response rate is much lower than in the current study, which can be explained by the fact that in Duma's study only radiation oncologists were asked to complete the survey instead of RTTs, radiation oncologists and medical physicists.

Another study the obtained results can be compared with is the study of Beaton et al. (2018). They investigated the treatment experience of patients treated with DIBH using the Elekta Active Breathing Coordinator (ABC) by means of a survey.(21) This technique uses a spirometer that monitors the airflow throughout the respiratory cycle. The device stops at a certain volume, and then the patient has to hold breath at this volume. To analyze the changes during the treatment, the survey was given to patients at three stages of the treatment. For example, in the survey was asked how comfortable the patients were with the ABC device. In general, patients indicated that they were comfortable. In the survey of the current study, respondents indicated that using 60%O<sub>2</sub> could have a big impact on patients. The study of Beaton et al. (2018) shows that the ABC device is not really stressful for patients. The ABC device is similar to the way of giving a patient 60%O<sub>2</sub>. To know the impact of 60%O<sub>2</sub> to a patient, a survey should be conducted among patients who are treated with 60%O<sub>2</sub>.

### **4.3 Strengths and limitations**

For this research, only one respondent per profession was asked per department. The results showed that there can be a lot of difference in answer between different professions in the same department. If this survey were repeated, more respondents per profession would be invited to get a higher reliability. In contrast, the departments with discrepancies in answers were telephoned to find out the right answer.

Another limitation might be that the survey was tested by RTTs only before inviting other departments, and not by radiation oncologists and medical physicists. To make the survey even stronger and to increase the validity, these professions also should have checked the survey. Perhaps this would provide different feedback than from the RTTs, which could have made the survey more complete.

The survey is completed by 70% of the research population. These respondents are divided over all main locations of radiotherapy departments in the Netherlands. This shows that the results are reliable to answer the research questions of this graduation assignment. This assignment is part of a bigger research project. With the results of this survey, the research group can continue their work in which further consideration is given to the application of 60%O<sub>2</sub>. By already generating some awareness about the use of 60%O<sub>2</sub> among the different professions in radiotherapy departments in the Netherlands, the transition to the actual introduction in clinical practice might be easier. In the Amsterdam UMC the concept survey circulated a lot to check it, so the use of 60%O<sub>2</sub> was already known to more people in this department. The use of 60%O<sub>2</sub> has been explained to the department and is already applied.

A strong aspect of this research is that three different professions per department were approached to complete the survey. This study benefits from the opinion of all three professions and ensure that the subject receives wide attention per department.

### **4.4 Generalizability**

The results have shown that the respondents think reasonably positively about the use of 60%O<sub>2</sub>. For this study, all radiotherapy departments in the Netherlands and three different professions per department were asked to complete the survey. This population is heterogeneous and the respondents do mostly have the same opinion, which indicates that the results can be generalized for everyone working in radiotherapy in the Netherlands.

The results of this study may also be relevant for departments abroad. They provide an overview of breath-hold techniques in the Netherlands and shows how RTTs, radiation oncologists and medical physicists envision the use of 60%O<sub>2</sub>. The same kind of breath-hold techniques are used abroad. As a consequence, patients there are also irradiated during free breathing. It is likely that RTTs, radiation oncologists and medical physicists in those countries will generally think similarly about the use of 60%O<sub>2</sub> as the respondents of this study.

## 5. Conclusion

Using this research, the secondary research questions have been answered, after which the main research question can be answered.

### 5.1 Secondary research question 1

*'How long are patients asked to hold their breath with how many breath-holds and which method is used in clinical practice in the Netherlands when patients with left-sided breast cancer are treated with DIBH?'*

The results to the survey questions showed that the mean breath-hold time used in the departments is 25 seconds, with an average of 8 breath-holds per treatment session. The most commonly method is voluntary breath-hold. The breath-hold is visually checked with a light field or by laser alignment with on the skin a reference mark.

### 5.2 Secondary research question 2

*'What percentage of patients with left-sided breast cancer who should be treated with DIBH during radiotherapy in the Netherlands, cannot perform DIBH and for what reasons?'*

The answers in the survey shows that 5% of the patients with left-sided breast cancer is treated during free breathing. The most common reason is because patients cannot hold their breath long enough.

### 5.3 Secondary research question 3

*'To what extent are RTTs, radiation oncologists and physicists willing to use 60%O<sub>2</sub> to enable patients who cannot breath-hold for 20-30s to hold their breath for the required duration?'*

The majority of the respondents sees advantages in using 60%O<sub>2</sub> to double breath-hold duration. Most of them do not see any difficulties. The radiation oncologists are mostly interested in using 60%O<sub>2</sub> for patients who cannot breath-hold for the required duration. The medical physicists are interested in using 60%O<sub>2</sub> for lung cancer patients.

### 5.4 Main research question

*'What are the main considerations and what kind of issues are encountered when using DIBH in clinical practice in the Netherlands when patients with left-sided breast cancer are treated with DIBH?'*

Treatment with DIBH usually takes place through voluntary breath hold using 8 breath-holds of 25 seconds. The benefits of using 60%O<sub>2</sub> are recognized, but the opinions are divided about the use in clinical practice. The percentage of patients who cannot breath-hold for the required duration is 5% with the most common reason that patients cannot hold their breath long enough.

## 6. Recommendations

A number of recommendations have emerged from the results of this study. These are presented below as recommendations for the client and supervisors in the Amsterdam UMC, location AMC and for the radiotherapy departments in the Netherlands.

First of all, it is useful when departments give patients more training and instruction about DIBH before they start the radiotherapy treatment with DIBH. The most mentioned reason why patients are treated during free breathing is because they cannot hold their breath long enough (75%). As you practice holding your breath, it should get better and better. After more practice, more patients would already achieve the minimum requested breath-hold time in a department.

Which would make the breath-hold even easier, especially for patients who cannot hold their breath long enough, is to use 60%O<sub>2</sub>. This research has shown that the RTTs, radiation oncologists and medical physicist are generally supportive about using 60%O<sub>2</sub>, but they do have some concerns about it. These are mostly arise of uncertainties and can be resolved. For example, the impact to patients is a much mentioned difficulty, but prolonging DIBH with 60%O<sub>2</sub> should be less tiring for patients because less DIBHs per fraction would be needed.

Before 60%O<sub>2</sub> is used in the departments, the procedure and the benefits must become clear to employees. After this, training sessions can be organized, in which the use of 60%O<sub>2</sub> will be explained and the employees can practice using it. Hereafter, patients can be irradiated using 60%O<sub>2</sub>.

If the departments are going to use 60%O<sub>2</sub> in treatments, further research is recommended. It must then be investigated whether the patients who were irradiated during free breathing (5%), can now be treated with DIBH. A survey could also be used for this. It is also important to find out about any difficulties so that a solution can be devised.

It is also recommended to investigate the use of 60%O<sub>2</sub> in other cancer patient groups. In the current study, the focus was on left-sided breast cancer, but the survey also showed the interest in using 60%O<sub>2</sub> in other cancer patient groups. For this group it should also be calculated what percentage of patients would benefit of the use of 60%O<sub>2</sub> and whether there are any difficulties.

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# Attachments

## Attachment 1: Information sheet and survey

### Information sheet about breath-holding with air and 60% oxygen:

Please read the information sheet before starting the survey.

The survey will take about 15 minutes to complete.

In clinical practice in the Netherlands, patients with left-sided breast cancer are asked to breath-hold for around 20 to 30 seconds using only room air. Research has shown that breath-hold duration is prolonged (at least doubled) by training (good technique of maximum inhalation and repeating this), and by breathing 60% O<sub>2</sub> instead of room air before the start of the breath-hold. It is shown in figure 1.

Breath-holding causes the systolic blood-pressure to increase, so this technique is not completely riskless, but the rising pressure is acceptable and easily monitored. Of these prolongation techniques, preparation with 60% O<sub>2</sub> without the use of a mechanical ventilator is easiest to apply, because this involves no sophisticated equipment.

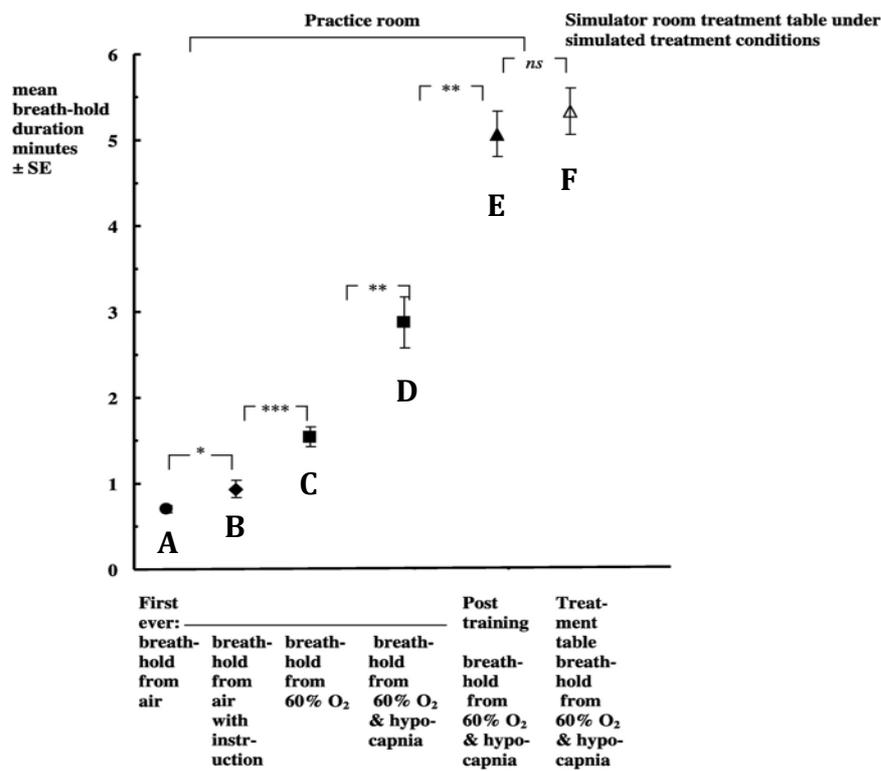


Figure 1: First ever breath-hold durations (A) in 15 breast cancer patients significantly improve after instruction (B) and after breathing 60% O<sub>2</sub> (C) instead of room air. D, E and F show increased breath-hold durations after non-invasive mechanical ventilation with 60% O<sub>2</sub> and hypocapnia

The use of 60% O<sub>2</sub> does not affect the systolic blood pressure. Using 60% O<sub>2</sub> is an easy, safe, inexpensive and universally applicable method which enables patients who cannot breath-hold for longer than 20-30s with room air, to hold their breath for more than twice as long.

The clinical gains from offering 60% O<sub>2</sub> to all patients to enable them performing longer breath-holds include the advantage of requiring fewer breath-holds per fraction. This would also be less tiring for patients and would increase their confidence. Furthermore, if all patients could hold their breath for a longer time, the smaller number of breath-holds per fraction could mean that more patients could be treated each day, which will lead to greater efficiency in clinical practice.

### **Survey:**

The questions in the survey which are not relevant for this thesis are shown in light grey. The answers are presented in Attachment 2.

### **General questions:**

1. In which radiotherapy department do you work?
2. Since when have you been working in this department?
3. What is your position in this department?
  - RTT
  - Radiation oncologist
  - Medical physicist

### **General questions about breath-hold:**

4. Which breath-hold technique (the method used) and what breath-holding equipment are used in your department when treating patients with left-sided breast cancer? (You may give more than one answer) (Nominal)
  - Active Breathing Control, with a spirometer that will monitor the airflow throughout the respiratory cycle. At a certain volume the device stops and the patient has to hold breath at this volume (go to question 6)
  - Real-time Position Management, an infrared camera is used and on the patient is placed a reflective marker to track the respiratory motion. A gating threshold is set when the patient reaches an acceptable volume (go to question 6)
  - Voluntary breath-hold, if the patient holds his breath, this is visually checked with a light field or by a laser alignment with on the skin a reference mark (go to question 6)
  - Breath-holding is not used (go to question 5)
  - Other, ... (please explain)
5. What is the reason breath-holding is not used in your department?

If breath-hold is not used in your department, go to question 18.

6. Do you ask patients to practice breath-holding before attending treatment? (Nominal)
  - Yes
  - No (go to question 10)
7. If you answered 'yes' to question 6, what kind of advice do they get? (You may give more than one answer) (Nominal)
  - Practice at home to hold your breath for a long time
  - Instructions during treatment consisting of "Take a few deep breaths and then hold your breath"
  - Other, ... (please explain)
8. At what moment are patient's given information or advice on breath-holding? (You may give more than one answer) (Nominal)

- On the CT scan day, just before the CT scan
  - On a previous day as a separate appointment to provide information
  - An information folder
  - Other, .... (please explain)
9. Who informs/advices the patients on breath-holding? (You may give more than one answer) (Nominal)
- RTT
  - Radiation oncologists
  - Other, ... (please explain)

**Detailed questions about breath-holding:**

10. What is the minimum breath-hold duration required from patients who are treated with DIBH? (Ordinal)
- 15s
  - 20s
  - 25s
  - 30s
  - 35s
  - 40s
  - 45s
  - 50s
  - More than 50s
11. How do you establish what is the minimum time each patient can hold their breath? (Nominal)
- The same inspiratory duration is required for all patients
  - On the CT, it is checked how long the patient manages to breath in and this time is also used during radiation.
  - Other, ... (please explain)
12. How long does an irradiation session with multiple DIBH take? (i.e. from the time the patient gets on the table until the time the patient gets off the table) (Ordinal)
- 5-10min
  - 10-15min
  - 15-20min
  - 20-25min
  - 25-30min
  - More than 30min
13. How many breath-holds are required on average for a complete irradiation session? (Including the imaging) (Ordinal)
- 1-3 breath-holds
  - 4-6 breath-holds
  - 7-9 breath-holds
  - 10-12 breath-holds
  - 13-15 breath-holds
  - 16-18 breath-holds
  - 19 or more breath-holds

14. How many patients with left-sided breast cancer do you treat annually with breath-hold? (An exact number is preferable. If this is not possible, then an estimated number is sufficient) (Continuous)
- Enter an exact number
  - Enter an estimate
15. How many patients with left-sided breast cancer do you treat annually during free breathing because they cannot perform DIBH? (An estimated number is sufficient) (Continuous)
- Enter an exact number
  - Enter an estimate
16. What is the most common reason patients are being treated with free breathing? (Nominal)
- They cannot hold their breath long enough
  - They cannot hold their breath at a constant inflation volume, which makes the breath-hold inconsistent
  - Patients cannot follow the instructions
  - Other, ... (please explain)
17. What other types of cancers do you treat with breath-holding? (You may give more than one answer) (Nominal)
- Stomach
  - Liver
  - Kidney
  - Pancreas
  - Spleen
  - Breast
  - Lung
  - Esophagus
  - Other, .....

**Breath-hold with 60% oxygen:**

18. Is an oxygen supply present in the treatment rooms? (Nominal)
- Yes
  - No
19. Has anyone explained to you the clinical advantages in doubling breath-hold duration with 60% O<sub>2</sub>? (Nominal)
- Yes
  - No

Please ensure you have read the accompanying information about breath-holding with 60% O<sub>2</sub>.

20. Can you see any clinical advantage in doubling breath-hold duration with 60% O<sub>2</sub>? (Nominal)
- Yes
  - No
21. What difficulties do you see in using 60% O<sub>2</sub> for breath-holding in addition to those difficulties answered in the information sheet?

22. Would you be interested to consider using 60% O<sub>2</sub> in the future to enable patients with left-sided breast cancer who cannot breath-hold for the required duration? (Nominal)
- Yes
  - No
23. Would you be interested to consider using 60% O<sub>2</sub> for patients with left-sided breast cancer? (Nominal)
- Yes
  - No
24. Would you be interested to consider using 60% O<sub>2</sub> for other cancer patient groups? (Nominal)
- Yes
  - No
25. If the answer to the previous question is yes, please specify for which cancer patient groups. (You may give more than one answer) (Nominal)
- Stomach
  - Liver
  - Kidney
  - Pancreas
  - Spleen
  - Breast
  - Lung
  - Esophagus
  - Other, .....
26. Would you like to receive more information about using 60% O<sub>2</sub> for breath-holding? (Nominal)
- Yes
  - No
27. If your answer to the previous question is yes, how would you like us to give you this information? (You may give more than one answer) (Nominal)
- Teams meeting
  - Visit
  - Documentation that we can send to you (please provide your e-mail details, ....)
  - Other, ...
28. Would you like to receive the results of the survey? (Nominal)
- Yes, e-mail: ...
  - No

*Nominal = A chosen variable from a list of variables.*

*Ordinal = The ranking of a variable relative to other variables in a list.*

*Continuous = Variables that can take any possible value.(14)*

## Attachment 2: Results of the remaining questions

The answers to the following questions (5-9, 11, 17-19, 26 and 27) are not reported in this thesis, since they do not directly address the main research questions, nor the secondary questions. These questions however are of interest for the bigger research project.

### 5. What is the reason breath-holding is not used in your department?

Breath-holding is used in all 20 photon radiation departments. The only departments not using breath-hold were proton centres.

### 6. Do you ask patients to practice breath-holding before attending treatment?

Practice before treatment	Number of departments (N=20)
	N (%)
Yes	15 (75)
No	5 (25)

### 7. If you answered 'yes' to question 6, what kind of advice do they get? (More answers possible)

Advice	Number of departments (N=15)
	N (%)
Practice at home to hold your breath for a long time	14 (93)
Instruction video at home	4 (27)
Instructions during treatment consisting of "Take a few deep breaths and then hold your breath"	13 (87)

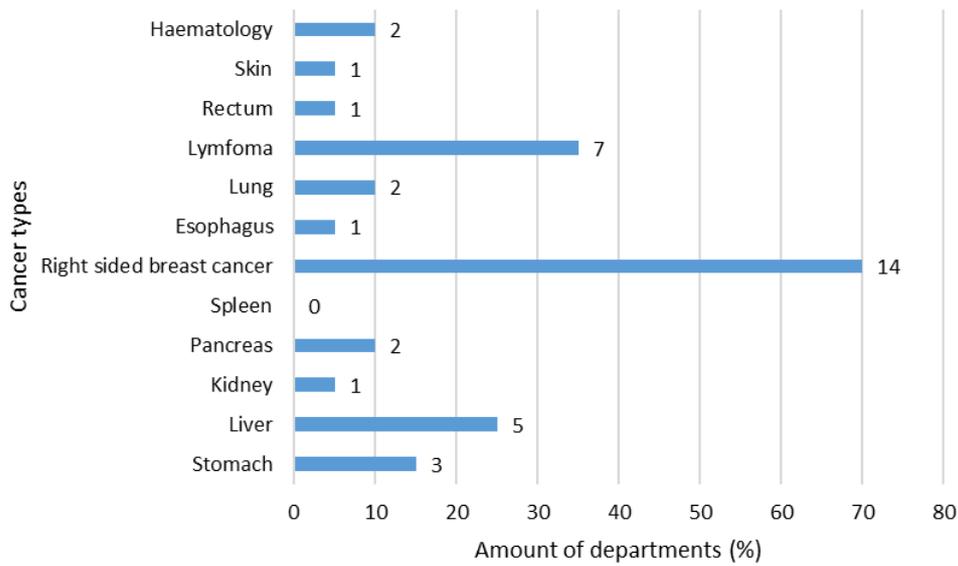
### 8. At what moment are patient's given information or advice on breath-holding? (More answers possible)

Moment of information	Number of departments (N=15)
	N (%)
An information folder	5 (33)
During the intake consult	2 (13)
On a previous day as a separate appointment to provide information	6 (40)
On the CT scan day, just before the CT scan	8 (53)

**9. Who informs/advices the patients on breath-holding? (More answers possible)**

Who informs/advices	Number of departments (N=15)	
	N	(%)
RTT	15	(100)
Radiation oncologist	7	(47)
Nurse practioners	1	(7)

**17. What other types of cancers do you treat with breath-holding? (You may give more than one answer)**



**18. Is an oxygen supply present in the treatment rooms? (Figure 12)**

Oxygen supply in treatment rooms	Number of departments (N=22)
	N (%)
Yes	9 (41)
No	6 (27)
Not in all treatment rooms	7 (32)

**19. Has anyone explained to you the clinical advantages in doubling breath-hold duration with 60% O2?**

Explained the clinical advantages	RTTs (N=23)	Radiation oncologists (N=13)	Medical physicists (N=10)
	N (%)	N (%)	N (%)
Yes	9 (41)	4 (31)	4 40
No	14 (61)	9 (69)	6 60

**26. Would you like to receive more information about using 60% O2 for breath-holding?**

More information	RTTs (N=23)	Radiation oncologists (N=13)	Medical physicists (N=10)
	N (%)	N (%)	N (%)
Yes	10 (43)	6 (46)	6 60
No	13 (57)	7 (54)	4 40

**27. If your answer to the previous question is yes, how would you like us to give you this information?**

Information	Number of respondents (N=22)
	N (%)
Teams	4 (18)
Visit	3 (14)
Documentation	20 (91)