getragen von:
Deutsches Krebsforschungszentrum
Universitätsklinikum Heidelberg
Thoraxklinik-Heidelberg
Deutsche Krebshilfe

UniversitätsKlinikum Heidelberg

Studienprotokoll Version 1 (08.02.2017)

Titel der Studie:	„NCT mobil – Smartphone-basierte Videotelefonate in der Onkologie“
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1. Summary

As a comprehensive cancer center, the Department of Medical Oncology at the National Center for Tumor Diseases (NCT) / University Hospital Heidelberg provides medical care for thousands of cancer patients each year. Many of our patients travel for more than an hour to reach our clinic. While this is justified for most visits, there are often short follow-up visits that do not necessarily require a physical face-to-face interaction between doctors and patients. Based on previous studies from other countries (see below), it can be expected that a telemedicine approach (i.e. patient-doctor interaction at a distance) in this setting can decrease patient travel time and patient costs while preserving the quality of medical care. However, to our knowledge, such an approach has never been tested in an oncological setting in Germany.

Therefore, we plan to evaluate feasibility, efficiency and patient satisfaction with a smartphone-based video-conferencing application for planned follow-up visits in N=60 outpatients from NCT (with an accepted dropout of 6 patients, therefore including 66 patients initially). Part 1 of the study is an exploratory, prospective, randomized, open-label study. We will offer this study to patients with a scheduled ambulatory follow-up visit at NCT. Patients will be randomized to receive either an "office visit" or a "video visit" as the intervention in this study. Afterwards, patients will be offered to participate in part 2: a single-arm observation study, where patients and doctors can agree to use the video-conferencing application on an individual basis for the rest of the study period. Both parts of the study will be concluded by a structured questionnaire.

End points are feasibility ("how many visits were successfully concluded"), time efficiency ("how long was total time investment for patients and physicians") and patient satisfaction. This study will be the first of its kind in Germany and will also be the first study to investigate a smartphone-based technical solution for telemedicine in medical oncology.

2. Contents

1. Introduction

Telemedicine refers to the use of "telecommunication systems to deliver health care at a distance" [1]. *Video consultations* are a part of telemedicine, referring to the interaction of patients and doctors via

real-time audio and video conversations at a distance. In medical oncology, video consultations can be used for follow-up visits and for application of chemotherapy [2-5]. The application of telemedicine in oncology has been termed *teleoncology [6-8]*.

For more than a decade, telemedicine has been applied to deliver specialized cancer care to rural populations of Canada [9], Norway [10], Australia [11] and several parts of the USA [4, 12, 13]. In these settings, patients typically use a dedicated videoconferencing setup at a rural health center that is connected to another unit at a tertiary cancer center several hundreds of kilometers away [5, 14]. Alternatively, patients are equipped with a portable videoconferencing setup which they can use at home [15]. It has been shown that patients and physician satisfaction with teleoncology video consultations is very high [8, 13, 15]. Other controlled studies have shown that teleoncology can reduce anxiety and depression and might provide an improved disease comprehension [16].

In summary, teleoncology is feasible, can be implemented even in small healthcare centers and leads to a high patient and provider satisfaction. However, to our knowledge, there is no study investigating the use of teleoncology in Germany. Compared to the above-mentioned countries (Canada, Norway, Australia, USA), Germany has very different legal requirements and the population might have different attitudes regarding teleoncology [17].

2. Aims of the study

At the outpatient clinics of the Medical Oncology department at NCT, thousands of cancer patients are treated annually and more than 19,000 treatments are administered. Many of these patients travel for more than an hour to reach our clinic. Teleoncology might be useful to reduce travel time and improve access to specialized cancer are in these patients. Therefore, our first objective is to investigate whether teleoncology can be implemented in our department. This would be the first trial demonstrating feasibility of teleoncology in a large cancer center in Germany. Also, for the first time, our trial would use a smartphone-based technology platform for video consultations. Most studies about teleoncology are more than five years old and use dedicated technical setups for videoconferencing. To establish this technical infrastructure requires time and is relatively costly. Nowadays, smartphones are ubiquitously used. Many of our middle-aged cancer patients use smartphones while they are at our outpatient clinic. Therefore, we plan to use a purely smartphone-based technical platform without the need for special technical equipment.

3. Study design

In general, patients who have a planned follow up visit within the next two days to two weeks are eligible. The intervention in this study is one “video visit” or “office visit” per patient. Consented patients will be randomized 1:1 in a “video visit” and an “office visit” arm (Figure 1). The “video visit” group will have their follow up

visit via the telemedicine platform. The "office visit" group will have their regular follow up visit in our clinic (standard of care). After the office or video visit (at time point T1), patients will complete the satisfaction questionnaire (Questionnaire Q1). Subsequently, all patients will be offered continued use of the telemedicine app for further follow up visits that might be necessary in the following months until the study closes. This second part of the study is a mere observation study and will be concluded by a second written questionnaire (Questionnaire Q2) and optionally a short phone interview (at time point T2). We also ask patients for consent to be contacted for a 15 min Telephone interview. The qualitative interview by phone with 10-15 patients aims at complementing the quantitative survey data with qualitative data about their user experience, benefits and potential concerns about using video visits on a regular basis.

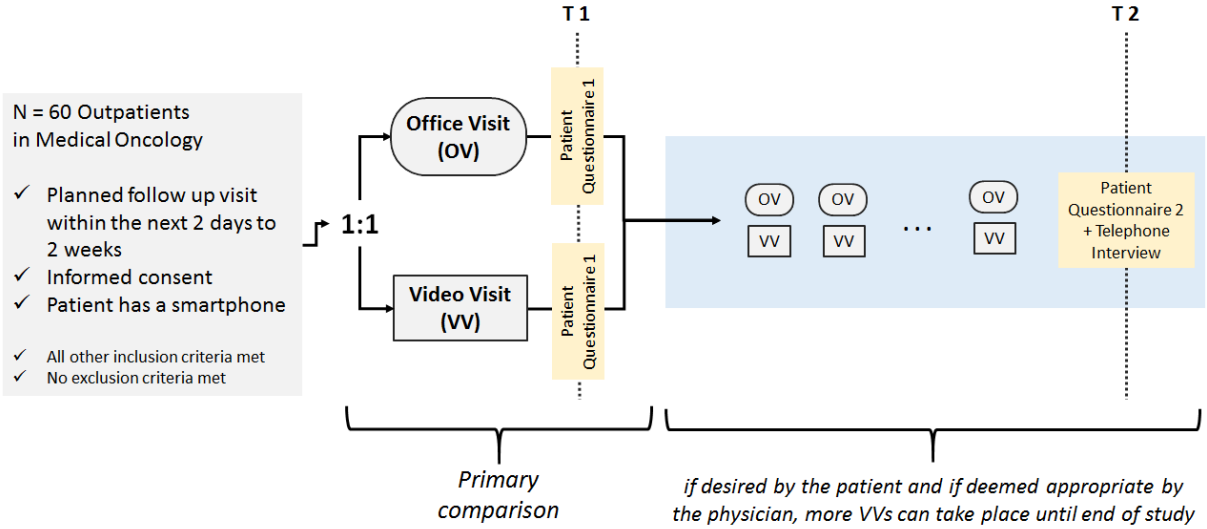

Figure 1: Visualization of the study design. We expect a 10% dropout and will therefore include 66 patients, so that at least 60 patients can be analyzed.

4. Outcome measures

This study is an explorative pilot study with several endpoints.

- **Feasibility:** Percentage of successfully completed visits: of all patients randomized to "video visit" or "office visit", how many do actually successfully complete this visit (measured at T1). A successfully completed visit is defined as a medical consultation between patent and doctor that is unanimously finished and is not cancelled because of technical issues or other problems.
- **Time-efficiency:** 1.) The total time needed for a single visit (from check in with the receptionist or launching the app to end of visit), as recorded by the patient. 2.) The total time needed for a single visit, excluding waiting time (from start to end of the patient-physician-interaction, as recorded by the physician).

- **Satisfaction with physician-patient interaction**: To assess patient satisfaction, we will quantitatively compare patient responses on the FAPI questionnaire at time point T1. The pooled sum of the response on all items will be used as an indicator of patient satisfaction.
- **Overall satisfaction with the experience with video visit and the technical platform (T2)**: At the end of the study (time point T2), all participants who participated in a video visit be surveyed with short self-developed questionnaire (and, optionally, a short telephone interview) about their experience in the study, their satisfaction with video visits in general and their satisfaction with the technical platform.

5. Data collection

In order to answer the above-defined questions, we will apply the following methods:

a) Collection of patient baseline data: For each patient, we will retrieve the following pieces of information from the hospital IT system (ISH-med): Age, gender, post code (to calculate distance to hospital), ICD-10 code of main oncological diagnosis, UICC stage of the tumor, time of diagnosis.
b) Assessing patient satisfaction, medical outcome and time per visit at time point T1: Patients will be asked to complete a self-developed questionnaire and the validated questionnaire FAP (both are part of Q1, attached)
c) Assessing patient satisfaction and overall experience with the telemedicine platform at time point T2: Patients will be asked to complete questionnaire Q2 (attached).
d) After each patient contact within this study, the physician will document the duration of the patient contact and provide a short summary on a paper-based case report form (CRF, attached). Patient data will be documented in a pseudonymized way by using the randomly attributed code generated at the beginning of the study. The actual patient identity will only be known to the study leaders and the physician who treats this respective patient.

6. Potential risks

The experimental intervention in the present study is a doctor-patient interaction either in a physical setting (office visit) or a telemedicine setting (video visit). In theory, the video visit might constitute a risk for the patient if the doctor misses important clinical information and makes a wrong clinical decision. However, to our knowledge, so far no such incidents have not been reported. Telemedicine in oncology has been shown to be safe even for therapeutic procedures (e.g. application of chemotherapy at a distance) [2-5]. Also, according to a Cochrane Review [1], telemedicine can be safely applied in a number of other situations (e.g. medical care for patients with heart failure or diabetes).

Furthermore, all participating physicians will be informed about the correct usage of the application and about the potential risks and limitations. If a physician is unsure whether a correct clinical decision can be made based on the information from the video chat, the patient will be asked to come to the clinic in person for an office visit or, in urgent cases, to seek medical help at the nearest emergency room.
Finally, the use of smartphones instead of dedicated hardware might constitute a potential risk. However, the software that will be used in this study is a professionally designed software that is already used by physicians in Germany and adheres to all relevant industry standards. Especially, all personal data and medical data are transferred in an encrypted way and are stored on servers in Germany (if they are stored at all). Of note, the video data itself is not stored, so the risk of data infringement is minimal.

7. Inclusion criteria patients

- Outpatients at the Medical Oncology Department, NCT (i.e. patients who had at least one face to face office visit before)
- Main diagnosis is a cancer disease
- ECOG 0-2
- Planned follow up visit within the next 2 days to 2 weeks
- Patient has a smartphone (iPhone or Android) and is comfortable using it
- Written informed consent for study participation
- Patient agrees with the terms and conditions for usage of the “Focus Health” application (attached)

8. Exclusion criteria patients

- Age < 18 years
- Not German-speaking
- Severe visual or auditory impairment

9. Inclusion criteria physicians

- Physicians from Medical Oncology at NCT who regularly see outpatients
- Willing to participate
- Physician has a smartphone (iPhone or Android) and is comfortable using it

10. Exclusion criteria physicians

- None

11. Randomization

At enrolment, patients will be randomized to either of the two arms by one of the two study leaders by opening a sealed randomization envelope. The envelopes will be prepared by the statistician. Block randomization will be used and everyone except the statistician is blinded with regard to the block length. The result of the randomization will be immediately written down in the study master file. Randomization will be requested by the physician responsible for this patient. The result of the randomization will be immediately communicated to the physician and the patient.

12. Sample size

Planned sample size is N=60 patients with N=30 patients in each group. We expect N=6 patients to be lost to follow up. Therefore, we will enroll N=66 patients in the study. The study will be closed as soon as the 66th patient has been enrolled. Due to the exploratory character of the trial, the planned sample size of 30 patients per group is solely based on matters of feasibility. Also, comparable previous studies included between 8 and 60 patients [13, 15, 18].

13. Practical aspects

Recruitment of physicians

Eligible physicians will be individually approached and offered to participate in the study. All participating physicians will be handed a copy of the study outline and all other relevant documents; they will be briefed about the correct usage of the application and will be provided with a personal user account. Each participating physician receives a unique ID within the application that will be exclusively communicated to his or her patients at enrolment. This is to ensure that patients can only connect to a physician who physically treated them before, in accordance with the "Berufsordnung für Ärzte". For this study, participating physicians can either use their own smartphone or a device provided by NCT according to their preference.

Recruitment of patients

Patients will be individually approached during one of their regular appointments at NCT. The treating physician provides the patient with written information material about the study and the technical platform used in the study and informs the patient about the aim of the study, the potential risks and limitations and about the practical aspects of the study. If the patient desires to participate, he or she will be asked for written informed consent (see "Patientenaufklärung" form, attached). Patients will be given written technical information on how to set up the application on their personal smartphone. If needed, they can request technical support by the official support team of the application's developers (Minxli) or from the study team at NCT.

Data and Documentation

Medical and/or personal data collected in this study is stored in the following ways:

- Within the smartphone application, as described in the privacy statement by the company (included in the patient information sheet)
- In our hospital information system ISH (all visits are documented in this system like all medical visits at NCT)
- On paper (clinical report forms and study master file), administered and stored by the study leaders

For all subsequent analyses, only pseudonymized data are used.

Statistical design and data analysis

Descriptive statistics will be used to evaluate baseline characteristics (mean, standard deviation, median, minimum, maximum for continuous, absolute and relative frequencies for categorical variables). The primary outcome feasibility, meaning "successfully complete the visit (yes/no)" will be described using absolute and relative frequencies. The groups will be compared by means of a chi-squared test at a (descriptive) two-sided significance level of $\alpha=0.05$. Additionally, a 95%-confidence interval for the rate difference between groups will be calculated.

Secondary outcomes will be descriptively assessed (mean, standard deviation, median, minimum, maximum for continuous, absolute and relative frequencies for categorical outcomes). Continuous outcomes will be compared using a two-sample t-test, while ordinal outcomes will be assessed using the Mann-Whitney U-test. For categorical outcomes, chi-squared test will be used to compare the two groups. The resulting p-values will only be interpreted in a descriptive manner.

The analysis follows the intention-to-treat approach, including all randomized patients regardless of any protocol violations. All analyses will be conducted using the statistical software SAS v9.4 or higher.

14. Exit criteria patients

- Withdrawal of consent for study participation
- Withdrawal of agreement with the terms and conditions for usage of the "Focus Health" application

If patients exit the study, they can decide whether the data collected up to this point can be used or if all collected data should be eliminated.

15. Exit criteria study

None.

16. Insurance for participants

Not required.

17. Compensation for health damage as a result of the study interventions

This study does not involve any potentially hazardous interventions.

18. Secure laboratory

Not required.

19. Potential conflict of interest

In this study, we will use the commercially available smartphone app "FocusHealth" by the company Minxli. Prior to the study, Minxli provided a for-free license and a test device to test the app. For the study, the Minxli will charge a reduced license fee. Other than that, no compensation whatsoever was provided. Minxli had no influence on study design.

20. Funding

We do not receive external funding for this study. Costs are limited to the license fee for the application, test devices for physicians and personell costs. All costs will be covered by our institution.

21. Attachments

1. Patient questionnaire Q1 (German)
2. Patient questionnaire Q2 (German)
3. Legal aspects of the study (German)
4. Patientenaufklärung (German)
5. Patient consent form (Einverständniserklärung, German)
6. Privacy statement for the smartphone application (German)
7. Case report form (CRF) template (German)

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