KANTONSSPITAL WINTERTHUR

Clinical Investigation Plan

EFFICACY OF MAGNETIC RESONANCE-GUIDED HIGH INTENSITY FOCUSED ULTRASOUND FOR THE ABLATION OF BREAST CANCER: CORRELATION BETWEEN MRI AND HISTOLOGY.

Single-Center, Single-Arm, Non-Randomized Trial

(CE-aequivalent documentation)

SHORT TITLE: MR guided HIFU for breast cancer

Study Type:	Intervention with Investigational Medical Device (IMD)
Study Categorization:	Clinical Trial with IMD Category C
Study Registration:	ClinicalTrials.gov Identifier: NCT03560102 Registration number (from BAG portal): BASEC 2017-01282, SWISSMEDIC 2017-MD-0021
Study Identifier:	
Sponsor-Investigator:	Prof. Dr. med. Christoph A. Binkert Kantonsspital Winterthur Institut für Radiologie und Nuklearmedizin Brauerstrasse 15 CH 8401 Winterthur Switzerland Phone: 0041 52 266 26 02 E-Mail: christoph.binkert@ksw.ch
Investigational Medical Device:	Philips Sonalleve MR-HIFU Breast Therapy System
Investigation plan Version and Date:	Version 1.1, 31. August 2017

STUDY SYNOPSIS

Sponsor / Sponsor-Investigator	Prof. Dr. med. Christoph A. Binkert
Study Title:	Efficacy of magnetic resonance-guided high intensity focused ultrasound for the ablation of breast cancer: correlation between MRI and histology.
Short Title / Study ID:	MR guided HIFU for breast cancer
Investigation Plan Version and Date:	Version V1.1 , 31. August 2017
Trial registration:	ClinicalTrials.gov Identifier: NCT 03560102 Registration number (BAG portal): BASEC 2017-01282, SWISSMEDIC 2017-MD-0021
Study category and Rationale	Clinical study with IMD Category C.
Clinical Phase:	Phase of development for medical device: Device is not CE or MD marked.
Background and Rationale:	The dedicated MR-HIFU unit has been shown to be safe and feasible to ablate breast tissue. The planned study should help to develop a minimal-invasive local therapy for breast cancer as an alternative treatment to surgery.
Objective(s):	The purpose of the study is to evaluate the efficacy of a dedicated MR-HIFU unit in ablating breast cancer with a non-invasive method. **Primary objective:** to evaluate the accuracy of MRI as a non-invasive method for assessment of treatment success. **Secondary objective:** Evaluation of treatment efficacy.
Outcome(s):	**Primary endpoint:** accuracy of MRI as method for assessment of qualitative and quantitative treatment success compared to the results of the histopathological analysis performed as reference method. **Secondary endpoint:** *evaluate treatment efficacy (necrosis of tumor and safety margin >1mm)*
Study design:	Single-center, single-arm, non-randomized trial

Inclusion / Exclusion criteria:	**Key inclusion criteria:** - Biopsy proven cT1-2 N0-2 MX invasive breast cancer with a size of ≤3.0cm. - Histological type of tumor: invasive ductal carcinoma (IDC) - Patient is scheduled for surgical resection of tumor at Kantonsspital Winterthur - Tumor location within the reach of the HIFU transducers with the patient in prone position; distance from skin and pectoral muscle to the tumor ≥ 1.0 cm. - Target breast fits in the cup of the dedicated MR-HIFU breast system - **Key exclusion criteria:** - neoadjuvant systemic therapy - prior radiotherapy in target breast - contraindications for study procedures - macro-calcifications in or around the targeted tumor - scar tissue or surgical clips in the direct path of the ultrasound beams - Women who are pregnant or breast feeding,

Measurements and procedures:	**Before treatment (Screening/Baseline):** - Tumor assessment by MRI (routine procedure) - Location of tumor site - Check of inclusion/exclusion criteria - Medical history - Demographics, height, weight, WHO performance status - Baseline assessment of pain - Pregnancy test for women of child-bearing potential. **Treatment (Study intervention):** Evaluations before MR-HIFU treatment: - Physical examination of breast - Assessment of pain - Assessment of adverse events - Assessment of changes in concomitant therapy Evaluations during MR-HIFU treatment: - DCE-MRI after treatment - Documentation of treatment parameters - Evaluations before discharge of patient: - Physical examination of breast - Assessment of pain - Assessment of adverse events - Assessment of changes in concomitant therapy **Follow-up (phone contact, day 2):** - Assessment of pain. - Assessment of adverse events - Assessment of changes in concomitant therapy **End of Study:** - DCE-MRI - Physical examination of breast - Assessment of pain - Assessment of adverse events - Assessment of changes in concomitant therapy **Surgery (non-study procedure):** Surgical ablation of the tumor (histopathological analysis of tumor tissue).

Study Product / Intervention:	**Study product:** Philips Sonalleve MR-HIFU Breast Therapy System **Study intervention:** The breast tumor lesion of qualified study patients will be treated with MR-HIFU under procedural sedation. Two follow-up DCE-MRI scans will be performed for evaluation of treatment efficacy. The first DCE-MRI is done directly after the MR-HIFU treatment (patient still in sedation). **Treatment time:** - MR-HIFU procedure including preparation and first DCE-MRI (2-3 hours) - Recovery time after procedure (ca. 3 hours). **Follow-up MRI:** The second DCE-MRI will be performed 8 (±2) days after treatment (ambulant procedure).
Control Intervention (if applicable):	not applicable
Number of Participants with Rationale:	This project is performed as a proof-of-concept study with a limited sample of 10 patients.
Study Duration:	Estimated duration of main investigational plan: 13 month (patient recruitment: 12 month; duration of individual patient participation 2-3 weeks)
Study Schedule:	First-Participant-In (planned): Q1/2018 Last-Participant-Out (planned): Q2/2019
Investigator(s):	Prof. Dr. med. Christoph A. Binkert Kantonsspital Winterthur Institut für Radiologie und Nuklearmedizin Brauerstrasse 15 CH 8401 Winterthur Switzerland Phone: 0041 52 266 26 02 E-Mail: christoph.binkert@ksw.ch
Study Centre(s):	Single-center study

Statistical Considerations:	This proof-of-concept study will be analyzed predominantly with methods of descriptive statistics. **Primary outcome:** Quantitative analysis: Comparison and correlation of results from histopathology and DCE-MRI regarding Size/Volume of tumor and volume/percentage of tumor necrosis Qualitative analysis: Comparison of results from histopathology and DCE-MRI regarding spatial congruence of ablated tumor tissue and width of margin **Secondary outcome:** Assessment of treatment efficacy (Effective treatment: complete necrosis of targeted tumor including safety margin (>1mm) **Safety analysis** AEs in general and additional predefined safety parameters will be presented by type and grade in tables showing frequency.
Statement:	This study will be conducted in compliance with the investigation plan, the current version of the Declaration of Helsinki, the ISO EN 14155 as well as all national legal and regulatory requirements.