


BMJ Open Protocol for the T-REX-trial: tailored regional external beam radiotherapy in clinically node-negative breast cancer patients with 1-2 sentinel node macrometastases – an open, multicentre, randomised non-inferiority phase 3 trial

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ABSTRACT

Introduction Modern systemic treatment has reduced incidence of regional recurrences and improved survival in breast cancer (BC). It is thus questionable whether regional radiotherapy (RT) is still beneficial in patients with sentinel lymph node (SLN) macrometastasis. Postoperative regional RT is associated with an increased risk of arm morbidity, pneumonitis, cardiac disease and secondary cancer. Therefore, there is a need to individualise regional RT in relation to the risk of recurrence.

Methods and analysis In this multicentre, prospective randomised trial, clinically node-negative patients with oestrogen receptor-positive, HER2-negative BC and 1-2 SLN macrometastases are eligible. Participants are randomly assigned to receive regional RT (standard arm) or not (intervention arm). Regional RT includes the axilla level I–III, the supraclavicular fossa and in selected patients the internal mammary nodes. Both groups receive RT to the remaining breast. Chest-wall RT after mastectomy is given in the standard arm, but in the intervention arm only in cases of widespread multifocality according to national guidelines. RT quality assurance is an integral part of the trial.

The trial aims to include 1350 patients between March 2023 and December 2028 in Sweden and Norway. Primary outcome is recurrence-free survival (RFS) at 5 years. Non-inferiority will be declared if outcome in the de-escalation arm is not >4.5 percentage units below that with regional RT, corresponding to an HR of 1.41 assuming 88% 5-year RFS with standard treatment. Secondary outcomes include locoregional recurrence, overall survival, patient-reported arm morbidity and health-related quality of life. Gene expression analysis and tumour tissue-based studies to identify prognostic and predictive markers for benefit of regional RT are included.

Ethics and dissemination The trial protocol is approved by the Swedish Ethics Authority (Dnr-2022-02178-01, 2022-05093-02, 2023-00826-02, 2023-03035-02). Results will be presented at scientific conferences and in peer-reviewed journals.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Prospective randomised trial, giving the highest level of scientific evidence.
- ⇒ Participation of multiple sites and countries.
- ⇒ The trial includes breast cancer patients with oestrogen receptor (ER)-positive, HER2-negative disease and 1-2 sentinel node macrometastases.
- ⇒ Prognostic and predictive markers will be investigated through tissue-based gene assays.
- ⇒ Limitation—ER-negative, HER2-positive and/or T3-4 tumours not included.

Trial registration number NCT05634889.

INTRODUCTION

Each year approximately 8000 Swedish, 4000 Norwegian and 5000 Finnish women are diagnosed with breast cancer (BC). Standard treatment for early BC is surgery combined with systemic therapy and radiotherapy (RT), which today commonly includes regional lymph nodes in case of lymph node metastases. Earlier BC trials have shown regional RT to approve prognosis for women with nodal disease on a group level.^{1 2} In the EORTC 22922/10925 trial there was a reduction in BC-mortality with regional RT after 15-year follow-up, and the MA.20 trial shows a reduction in BC-recurrences after 10 years.^{3 4} However, modern systemic therapy has significantly improved survival and decreased the incidence of locoregional recurrences. Regional recurrences are therefore today rare events,^{5–9} and it is being questioned whether regional RT still have the same benefit for low-risk patients with limited nodal disease.



Current treatment recommendations on regional RT differ between countries and sites, both regarding included lymph node levels (axilla level I–III, supraclavicular and/or internal mammary nodes (IMN)) and patient selection. Regional RT is associated with a risk of complications such as arm morbidity, skin irritation, pneumonitis, cardiac disease, second cancers (lung cancer, angiosarcoma, oesophageal cancer) and hypothyroidism.^{10–15} RT also significantly deteriorates surgical and patient-reported outcomes of breast reconstruction.^{16 17} There is therefore a need for modern data on risks and benefits associated with regional RT, thus providing an opportunity to customise its use in relation to the individual risk of recurrence.

The ACOSOG Z0011 trial randomised patients with T1–2 invasive BC and 1–2 sentinel lymph node (SLN) metastases, treated by breast-conserving surgery (BCS) and whole-breast RT, to axillary lymph node dissection (ALND) or no further axillary treatment.¹⁸ The axillary recurrence rate was low, and there was no significant survival difference between the randomisation groups after 9 years of follow-up. In a retrospective analysis on 228 available RT plans (29%), out-of-protocol regional RT had been given to 19% of patients, and in an additional ~40%, breast RT included high tangential fields covering large parts of axillary levels I–II, that is, 50%–90% of levels I–II received 95% of the prescribed dose.¹⁹ It is therefore questionable whether ACOSOG Z0011 can guide clinical practice regarding the safe omission of ALND in patients with 1–2 SLN macrometastases without the addition of regional RT.

The AMAROS trial, on the other hand, included patients with T1–2 invasive BC and 1–2 SLN metastases, and randomised between ALND or regional RT. RT included all levels of the axilla and the medial supraclavicular nodes. No significant differences in survival or recurrence rate between the randomisation groups have been reported after 10 years of follow-up.^{15 20} Both ALND and axillary RT provided equally excellent locoregional control. While lymphoedema was more commonly seen in the ALND-arm, the group receiving axillary RT had a higher incidence of difficulties in moving the arm.⁸

Additional trials indicating the feasibility to de-escalate regional treatment in BC are IBCSG 23–01,²¹ OTOASOR,⁵ OPTIMAL,⁶ RAPCHEM,⁹ NSABP-04²² and the SINODAR-ONE trial.⁷ Results are also awaited from the Swedish SENOMAC-trial.^{23 24} Collectively, these trials have introduced omission of ALND as an option in patients with limited axillary lymph node involvement. It is, however, still unclear whether regional RT to the undissected axilla, supraclavicular nodes and IMN need to be part of locoregional treatment in these patients.

Currently, there is one ongoing and one completed, but not yet reported, randomised trial addressing the therapeutic value of regional RT in addition to SLN biopsy in clinically node-negative (cN0) patients with limited axillary involvement. In the POSNOC trial, patients with early BC and 1–2 SLN macrometastases are randomised

between one modality of axillary treatment (ALND or regional RT) and surveillance only. In the MA.39 trial, on the other hand, women with low-risk BC (oestrogen receptor (ER) positive, HER2-negative, OncotypeDX score <18) are randomised after SLN biopsy or ALND between regional RT and no regional RT; 1–3 macrometastases are allowed after ALND and 1–2 after SLN biopsy alone.

In order to change international guidelines, however, additional data are needed which compare the currently most common treatments, that is, SLN biopsy followed by regional RT or SLN biopsy alone, as in the planned T-REX trial. In addition, the translational protocol of the T-REX trial aims to decipher the prognostic and predictive role of tumour biology and gene expression analysis for their potential integration into future adjuvant RT individualisation.²⁵

Hypothesis

Refraining from regional RT in cN0 BC patients with 1–2 sentinel node macrometastases and T1–2 tumours, ER-positive and HER2-negative disease does not worsen 5-year recurrence-free survival (RFS).

Refraining from regional RT reduces arm morbidity and late RT side effects such as heart disease and non-BC malignancies (lung cancer, angiosarcoma), and potentially improves short-term and long-term health-related quality of life (HRQoL).

Genomic classifiers can prognosticate locoregional recurrences and predict benefit from regional RT, which can be used to guide future individualised adjuvant regional RT.

METHODS AND ANALYSIS

Overall trial design

T-REX is a prospective, multicentre, open phase 3 trial (figure 1). cN0 BC patients with 1–2 SLN macrometastases and an ER-positive, HER2-negative T1–2 tumour receiving primary surgery (no neoadjuvant systemic treatment) are randomised to standard regional RT versus no regional RT. All patients will receive RT to the remaining breast after breast conserving surgery. Mastectomy patients in the intervention arm will not receive any RT, with the exception if chest wall RT is indicated due to tumour multifocality according to national guidelines.

Arm A

Regional RT (standard): RT to the remaining breast after BCS or chest wall after mastectomy, axillary lymph nodes (levels I–III) and supraclavicular lymph nodes (level IV). IMN are included in the target volume according to national guidelines.

Arm B

No regional RT, that is, no lymph node levels included in the target volume. RT is given to the remaining breast after BCS. No chest wall irradiation after mastectomy.

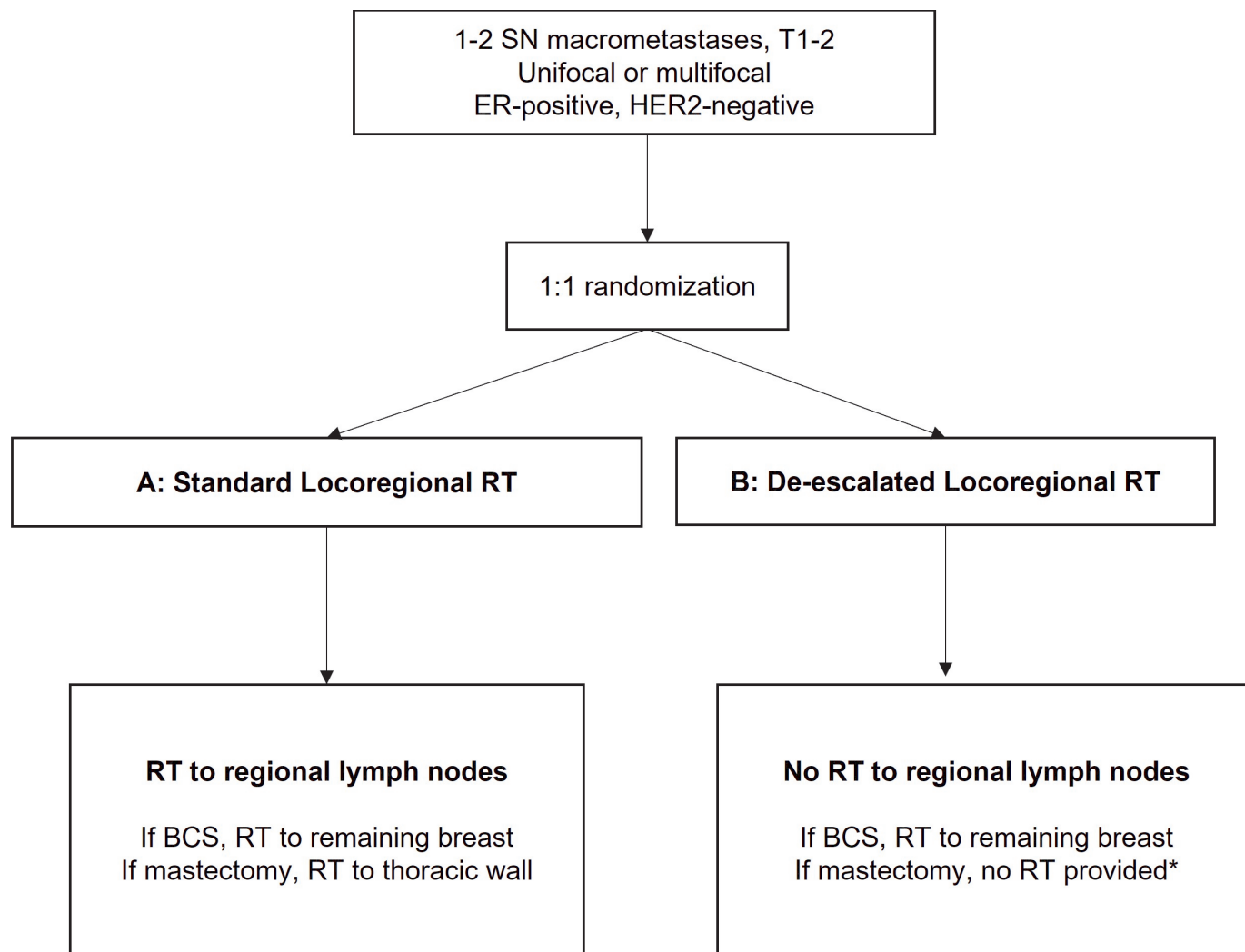


Figure 1 Trial design. *Exception - chest wall irradiation in the intervention arm is permitted in cases of extensive multifocality, as recommended by national guidelines. BCS, breast-conserving surgery; ER, oestrogen receptor; RT, radiotherapy; SN, sentinel node.

However, an exception is that chest wall irradiation is permitted in cases of extensive multifocality, as recommended by national guidelines.

Trial population

After surgery, cN0 BC patients with T1-2, ER-positive, HER2-negative tumours and 1-2 SLN macrometastases are screened for eligibility. All histological tumour subtypes are eligible, and both tumour multifocality and additional SLN micrometastases are allowed. Only gross but not microscopic extracapsular extension excludes candidates from the trial. Patients who have undergone ALND or have received neoadjuvant systemic treatment prior to surgery are ineligible for the trial. Inclusion and exclusion criteria are shown in [table 1](#).

Patients are screened for eligibility within 4–5 weeks after surgery. Trial information and invitation to participate will be given by a physician at a postoperative visit at the department of surgery or oncology. The overall trial procedure is shown in [figure 2](#).

After confirmation of eligibility and written informed consent (online supplemental file 1), patients are randomised 1:1 between treatment arms using a permuted block technique. Allocation is stratified by trial site and breast surgery (BCS vs mastectomy). Participation in T-REX should not affect or change decisions on systemic adjuvant treatment. Hence, systemic adjuvant treatment should be planned and documented before randomisation according to best standard of care, taking age and comorbidity into consideration. Furthermore, it should be confirmed that the patient is willing and able to adhere to such recommended systemic therapy before inclusion in T-REX.

Locoregional RT is given 5 days per week with 15 fractions of 2.67 Gy to a total target dose of 40.05 Gy. The same fractionation is used for whole-breast RT. However, in women >50 years who shall receive whole-breast RT without a tumour bed boost, and without inclusion of nodal fields, an alternative treatment scheme may be 5 fractions of 5.2 Gy to a total target dose of 26.0 Gy. In

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
<ol style="list-style-type: none"> 1. Primary unifocal or multifocal invasive breast cancer T1-T2 2. Clinically N0 3. Macrometastasis (>2 mm) in 1-2 lymph nodes at sentinel node biopsy 4. Oral and written consent 5. Age ≥18 years 6. Tumour-free resection margins (no tumour on ink) 7. Primary tumour ER-positive, HER2-negative 	<ol style="list-style-type: none"> 1. Regional or distant metastases outside the ipsilateral axilla 2. Previous RT towards the planned target area, that is, the ipsilateral chest/lymph nodes 3. Neoadjuvant systemic therapy 4. Axillary lymph node dissection or other previous axillary surgery on the affected side 5. History of invasive breast cancer 6. Pregnancy 7. Bilateral invasive breast cancer 8. Contraindication for radiotherapy or systemic treatment, if indicated. Hence endocrine treatment, chemotherapy and/or targeted therapy should at inclusion be planned to be given according to standard of care, taking age and comorbidity into consideration 9. Inability to absorb or understand the contents of the informed consent form; for example, through disability, insufficient language skills or dementia 10. Other invasive cancer within 5 years prior to breast cancer diagnosis

ER, oestrogen receptor; RT, radiotherapy.

accordance with the Fast Forward trial and Swedish National Guidelines.^{26 27} Tumour bed boost, IMN-RT and chest wall RT due to multifocality is given according to national guidelines.

Outcomes

Primary outcome

RFS at 5 years. RFS is measured from the date of randomisation until the date of first local recurrence, regional recurrence, distant recurrence or death by any course.

Secondary outcomes

Oncological outcomes:

- ▶ Locoregional recurrence.
- ▶ Overall survival, distant RFS.
- ▶ Contralateral BC.

Treatment-related outcomes:

- ▶ Arm morbidity at 1, 3 and 5 years assessed through the 'Lymphedema Functioning, Disability and Health Questionnaire' developed by Devoogdt in 2011.
- ▶ Quality of life assessed through EORTC questionnaires QLQ-30 and BR-23 at 1, 3 and 5 years. In

addition, sense of coherence will be evaluated at baseline through the SOC-13 questionnaire.

- ▶ Cardiac morbidity and incidence of non-breast malignancies (such as lung cancer and angiosarcoma) will be assessed using register data.

Tissue collection and analysis

When signing the informed consent form, participants will explicitly grant or abstain from permission for tissue collection, handling and biobanking/storage, and the use of such tissue in gene expression assays and translational analyses. For patients who agree to this, tissue from the primary tumour, surrounding stromal tissues and lymph node metastases will be collected and stored at a trial biobank in Gothenburg, Sahlgrenska University Hospital. Tissue samples from any recurrences during follow-up will be also collected.

Collected tumour tissues will be used for molecular analyses including gene expression signatures in order to identify genomic classifiers which can prognosticate locoregional recurrences and predict benefit from regional RT.

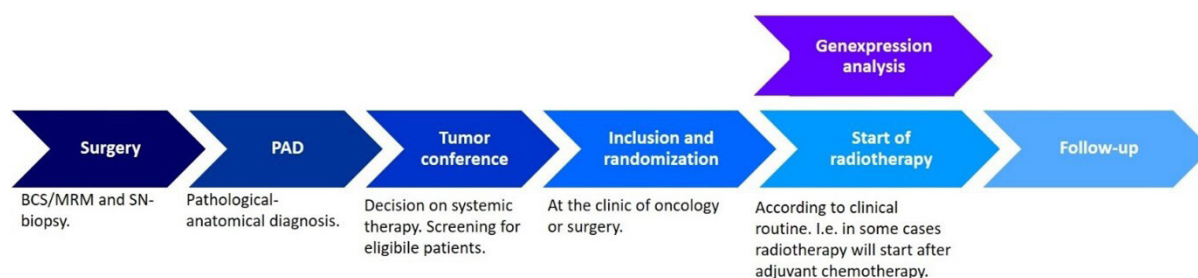


Figure 2 Trial procedure. BCS, breast-conserving surgery; MRM mastectomy; SN, sentinel node.

Table 2 Flow chart of follow-up

	Screening	Baseline	End of RT	1 year*	3 years*	5 years*	10 years*
	After surgery	Before start of RT	±2 months	±2 months of randomisation date			
Verify eligibility	X						
Obtain informed consent							
Randomisation	X						
Register patient and tumour characteristics†		X					
Register breast reconstruction data		X	X	X	X	X	X
Register adjuvant systemic therapy‡			X	X	X	X	X
Register detailed RT data			X				
Register recurrences and death				X	X	X	X
Arm morbidity questionnaire (Lymph-ICF)		X		X	X	X	
HRQoL questionnaires (EORTC QLQ-C-30 and BR-23)		X		X	X	X	
Sense of coherence questionnaire (SOC-13)		X					
Tumour tissue sent to biobank		X					

*All relevant information may be retrieved by physical visits or telephone contact with the participant, and/or through review of medical chart according to each site's routine.
 †Including demography, height, weight, waist and hip circumference, preoperative breast size, smoking history, current nicotine use and biomarker data.
 ‡Adjuvant systemic therapy should be given according to standard of care.
 Lymph-ICF, Lymphedema Functioning, Disability and Health Questionnaire; RT, radiotherapy.

Follow-up and quality assurance

Patients will be followed prospectively according to each site's clinical routine and participating countries' national guidelines. That is, no specific follow-up modality or schedule is postulated. Assessment of disease recurrence and questionnaire results for patient-reported arm morbidity and HRQoL will be registered in the electronic case report form (eCRF) at baseline, year 1, 3, 5 and 10 (table 2).

The trial will be monitored by independent monitors to ensure that it is carried out according to the protocol and that data is collected, documented and reported according to good clinical practice and applicable ethical, legal and regulatory requirements.

Further, an RT quality assurance (QA) programme is an integral part of the trial. Before entering, each centre will need to submit a benchmark delineation case for a left sided locoregional treatment including IMN. Treatment planning will be reviewed in conjunction with the RT for at least three patients from each centre: the first recruited left sided breast patients with breast only, locoregional without IMN and locoregional with IMN, respectively.

RT-related data are reported in the eCRF by each centre for all patients. Data in DICOM format (CT images, dose plan, dose distribution and structures) as well as a treatment report from the oncology information system is

collected by the QA centre for all Swedish patients and potentially for selected centres in other participating countries. This will be used to on a group level investigate dose to individual lymph node levels in the respective treatment arms. For patients with locoregional recurrence, a detailed described of its position in relation to previous RT-fields and dose will be given.

Time plan

The trial has started inclusion March 2023. First publication regarding QoL is planned for 2025–2026. End of inclusion is estimated to 2028 and publication of the primary endpoint 5-year RFS to 2033.

Participating countries and sites

The trial will initially include patients in Sweden and Norway, with the plan to extend inclusion also to Finland. In addition, the trial is open for adding further countries in the future. A full list of currently recruiting sites can be retrieved from the clinical trials office (cto.hematologi_onkologi.sus@skane.se).

Patient and public involvement

Patient representative Jaana Korkeamäki of the Swedish Breast Cancer Association's steering committee is member of the T-REX trial steering committee. She has

taken active part in preparing the trial protocol and the informed consent form and will be updated and involved in every stage of the trial.

Statistics, power calculations and data analysis plan

The aim of T-REX is to establish that the intervention (no regional RT), is statistically non-inferior to standard of care (regional RT) for the primary endpoint RFS. Clinical non-inferiority is defined as a 5-year RFS not worsened by more than 4.5 percentage units when refraining from regional RT. The non-inferiority margin was chosen with consideration of similar ongoing trials on axillary treatment in BC, for example, the Alliance trial and NSABP B-51 (non-inferiority margins 6 versus 4.6 percentage units, respectively, NCT01901094, NCT01872975).

Calculations are based on the assumptions of constant incidence of RFS events and a 5-year RFS of 88.0% in the standard arm, corresponding to the estimated 5-year RFS of the SENOMAC trial (www.senomac.se, currently unpublished data).

Assuming uniform inclusion during 5 years plus 5 years follow-up after completed inclusion, a total of 1221 patients need to be included in the trial to have 80% power to show that the 5-year RFS is not worsened by more than 4.5 percentage units (ie, a 5-year RFS of 83.5% in the intervention group compared with 88.0% in the standard group), using a one-sided test at the α level 5%. The 1221 patients should correspond to 213 events contributing to RFS. Drop-outs will not be replaced by a new randomisation. Hence, to allow for a drop-out of 10%, 1350 patients will be included. However, with the addition of more sites the trial opens for the possibility to include up to 1800 patients, which would yield statistical power for the primary endpoint to be reached already after 3 years of follow-up.

The primary analysis will be an unadjusted Cox regression with stratification for site based on the per-protocol population. However, primary outcome will also be evaluated in the intention to treat population. Since treatment is allocated randomly, adjustment for confounding will not be applied. Proportional hazards over the follow-up time will be assumed. Under the assumptions specified in the power calculation and exponentially distributed survival times, a non-inferiority margin of 4.5 percentage units translates to an upper limit of a one-sided 95% CI of 1.41 for the RFS-HR for regional RT versus no regional RT. Non-inferiority can be claimed if the upper limit does not exceed this value.

Homogeneity of treatment effect, intervention versus standard of care, will be analysed for subgroups based on age, BC stage, etc, and presented as forest plots. A Kaplan-Meier graph will be used to visualise the effect of treatment on RFS. Extensive monitoring should keep the rate of missing values for key variables low. Hence imputation techniques will not be applied. Patients who withdraw their informed consent or are lost to follow-up will be censored from the trial at this point.

An independent data safety monitoring committee will carry out a safety analysis 3 years after randomisation of the first patient, or when 500 patients have been included, whichever comes first. This is to assess recruitment rates, RFS events per group, and to make sure that patients in the intervention group do not appear to fare significantly worse than those in the standard group. The committee may recommend prematurely terminating the trial if a significant benefit in favour of standard of care for RFS is shown, such that the HR for intervention versus standard of care significantly ($p < 0.001$) exceeds 1, or if the recruitment is so low that the necessary number of events is unlikely to be reached.

Ethics and safety considerations

Based on older studies, an increased risk of recurrence among individual patients who do not undergo regional RT after ALND cannot be ruled out. However, several modern-era de-escalation trials have not shown any significant difference in survival or recurrences between trial arms. In addition, newer studies report generally improved survival and lower rates of locoregional recurrences compared with older ones, presumably due to improved systemic therapy, although a direct effect of RT cannot be excluded. In T-REX, eligibility is based on a low-risk profile regarding locoregional recurrence according to validated clinical markers such as tumour size, number of lymph nodes involved, ER and HER2 status.²⁸ Abstaining from regional RT for part of the patient population eligible for T-REX is already clinical routine in a number of countries. All study participants will be monitored for recurrences and receive treatment as indicated. In addition, a safety analysis will be performed as described earlier.

The possible risks of abstaining from RT must be weighed against significant benefits. BC patients have a long expected survival, and it is of utmost importance to keep long-term side effects to a minimum. Furthermore, RT is associated with a risk of acute and late side effects, such as skin toxicity, pneumonitis, arm morbidity, cardiac disease, lung cancer, angiosarcoma and hypothyroidism.^{10–14} The possibility to abstain from regional RT in patients with a low risk of regional recurrence would reduce side effects and lead to reduced morbidity, improved working ability and possibly increased HRQoL. Mastectomy patients would be spared 3 weeks daily visits to the RT department, and in patients receiving breast reconstruction, the significant risk of short-term and long-term complications and poor cosmesis associated with RT would be reduced. For patients operated with BCS, not adding regional RT to whole-breast irradiation would reduce treatment time from 3 weeks to 1 week if giving 5.2 Gy \times 5 fractions to a total dose of 26 Gy in accordance to the Fast Forward trial.²⁶ Finally, refraining from regional RT will save healthcare resources due to reduced work load in the hospitals.

The current benefit of regional RT in patients with limited SLN macrometastasis is unclear, and treatment

guidelines differ between countries and sites. There is therefore a need to explore this question through a randomised trial such as T-REX. In addition, gene expression analyses will be performed in order to determine their value in relation to prediction of locoregional recurrence, and for decision on adjuvant RT in the future.

This trial protocol (version 1.2, 5 May 2023) has been approved by the Swedish Ethics Authority (Dnr 2022-02178-01, 2022-05093-02, 2023-00826-02 and 2023-03035-02), and ethical permission is currently being applied for in Norway (decision expected September 2023). Furthermore, we intend to extend the trial to centres in Finland. The trial will be carried out in accordance with The Code of Ethics of the World Medical Association. All patients will sign an informed consent form before randomisation and will be free to withdraw from the trial at any time. The academic study steering committee will have ultimate authority over study design; collection, management, analysis and interpretation of data; writing of the report; and the decision to submit the report for publication. This will not be affected by current or possible future funders or industrial collaborators in translational projects.

Dissemination plan

Results from the primary and secondary endpoints are planned to be published in scientific peer-reviewed journals, and at scientific conferences. Important protocol modifications will immediately be communicated to relevant parties (eg, investigators, trial participants, trial registries, regulators, etc).

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Contributors All authors have made a substantial contribution to the conception and/or design of the work; and/or the acquisition, analysis, or interpretation of data for the work. All authors have participated in drafting the work and reviewing it critically. All authors have approved the final version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Their individual roles and contributions are specified here. SA: primary investigator of the trial; planned the trial and drafted the study protocol; main author of manuscript and study protocol. JdB: part of the trial steering committee; planned the trial and drafted the study protocol; participated in drafting the manuscript and reviewing it critically. PK: part of the trial steering committee; planned the trial and drafted the study protocol; participated in drafting the manuscript and reviewing it critically. DL: part of the trial steering committee; planned the trial and drafted the study protocol; participated in drafting the manuscript and reviewing it critically. LR:

part of the trial steering committee; planned the trial and drafted the study protocol; participated in drafting the manuscript and reviewing it critically. IM: part of the trial steering committee; planned the trial and drafted the study protocol; primary investigator for Norway; participated in drafting the manuscript and reviewing it critically. EW: part of the adjunct steering committee; responsible for writing the radiotherapy appendix in the study protocol and planning of radiotherapy quality control; participated in drafting the manuscript and reviewing it critically. JV: part of the Norwegian trial steering committee; responsible medical physicist for Norway; participated in writing the radiotherapy appendix in the study protocol and planning radiotherapy quality control; participated in drafting the manuscript and reviewing it critically. P-OB: part of the adjunct steering committee; trial statistician, responsible for statistical calculations in the study protocol; planned the trial and drafted the study protocol; participated in drafting the manuscript and reviewing it critically. EH: part of the adjunct steering committee; trial statistician, responsible for statistical calculations in the study protocol; participated in drafting the manuscript and reviewing it critically. HS: part of the adjunct steering committee; responsible for health-related quality of life assessments and questionnaires regarding arm morbidity specified in the study protocol; participated in drafting the manuscript and reviewing it critically.

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Competing interests SA has received honorary for lecturing for Astra Zeneca. LR has received honorary for lecturing from Onkologisk tidskrift, Denmark. PK and EH has contract with PFS Genomics/Exact Sciences regarding genomic profiling, are coinventor on patent applications, and have a contract with Prelude Dx.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

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REFERENCES

- McGale P, Taylor C, *et al*. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *Lancet* 2014;383:2127–35.
- Budach W, Bölke E, Kammers K, *et al*. Adjuvant radiation therapy of regional lymph nodes in breast cancer - a meta-analysis of randomized Trials- an update. *Radiat Oncol* 2015;10:258.
- Whelan TJ, Olivetto IA, Levine MN. Regional nodal irradiation in early-stage breast cancer. *N Engl J Med* 2015;373:1878–9.



- 4 Poortmans PM, Weltens C, Fortpied C, *et al.* Internal mammary and medial supraclavicular lymph node chain irradiation in stage I-III breast cancer (EORTC 22922/10925): 15-year results of a randomised, phase 3 trial. *Lancet Oncol* 2020;21:1602–10.
- 5 Sávolt Á, Péley G, Polgár C, *et al.* Eight-year follow up result of the OTOASOR trial: the optimal treatment of the axilla - surgery or radiotherapy after positive sentinel lymph node biopsy in early-stage breast cancer: a randomized, single centre, phase III, non-inferiority trial. *Eur J Surg Oncol* 2017;43:672–9.
- 6 Algara M, Rodríguez E, Martínez-Arcelus FJ, *et al.* Optimizing irradiation through molecular assessment of lymph node (OPTIMAL): a randomized clinical trial. *Radiother Oncol* 2022;176:76–82.
- 7 Tinterri C, Gentile D, Gatzemeier W, *et al.* Preservation of axillary lymph nodes compared with complete dissection in T1-2 breast cancer patients presenting one or two metastatic sentinel lymph nodes: the SINODAR-ONE multicenter randomized clinical trial. *Ann Surg Oncol* 2022;29:5732–44.
- 8 Coles CE, Griffin CL, Kirby AM, *et al.* Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial. *Lancet* 2017;390:1048–60.
- 9 de Wild SR, de Munck L, Simons JM, *et al.* De-escalation of radiotherapy after primary chemotherapy in Ct1-2N1 breast cancer (RAPCHEM; BOOG 2010-03): 5-year follow-up results of a Dutch, prospective, registry study. *The Lancet Oncology* 2022;23:1201–10.
- 10 Taylor C, Correa C, Duane FK, *et al.* Estimating the risks of breast cancer radiotherapy: evidence from modern radiation doses to the lungs and heart and from previous randomized trials. *J Clin Oncol* 2017;35:1641–9.
- 11 Killander F, Wieslander E, Karlsson P, *et al.* No increased cardiac mortality or morbidity of radiation therapy in breast cancer patients after breast-conserving surgery: 20-year follow-up of the randomized Swebcgrt trial. *Int J Radiat Oncol Biol Phys* 2020;107:701–9.
- 12 Wennstig A-K, Wadsten C, Garmo H, *et al.* Long-term risk of ischemic heart disease after adjuvant radiotherapy in breast cancer: results from a large population-based cohort. *Breast Cancer Res* 2020;22:10.
- 13 Huang H, Roberson J, Hou W, *et al.* NTCP model for hypothyroidism after supraclavicular-directed radiation therapy for breast cancer. *Radiother Oncol* 2021;154:87–92.
- 14 Karlsson F, Granath F, Smedby KE, *et al.* Sarcoma of the breast: breast cancer history as etiologic and prognostic factor-A population-based case-control study. *Breast Cancer Res Treat* 2020;183:669–75.
- 15 Bartels SAL, Donker M, Poncet C, *et al.* Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer: 10-year results of the randomized controlled EORTC 10981-22023 AMAROS trial. *J Clin Oncol* 2023;41:2159–65.
- 16 Ho AY, Hu ZI, Mehrara BJ, *et al.* Radiotherapy in the setting of breast reconstruction: types, techniques, and timing. *Lancet Oncol* 2017;18:e742–53.
- 17 de Boniface J, Coudé Adam H, Frisell A, *et al.* Long-term outcomes of implant-based immediate breast reconstruction with and without radiotherapy: a population-based study. *Br J Surg* 2022;109:1107–15.
- 18 Giuliano AE, Ballman KV, McCall L, *et al.* Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: the ACOSOG Z0011 (alliance) randomized clinical trial. *JAMA* 2017;318:918–26.
- 19 Jaggi R, Chadha M, Moni J, *et al.* Radiation field design in the ACOSOG Z0011 (alliance). *J Clin Oncol* 2014;32:3600–6.
- 20 Donker M, van Tienhoven G, Straver ME, *et al.* Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncol* 2014;15:1303–10.
- 21 Galimberti V, Cole BF, Zurrada S, *et al.* Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. *Lancet Oncol* 2013;14:297–305.
- 22 Fisher B, Jeong JH, Anderson S, *et al.* Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. *N Engl J Med* 2002;347:567–75.
- 23 de Boniface J, Ahlgren J, Andersson Y, *et al.* The generalisability of randomised clinical trials: an interim external validity analysis of the ongoing SENOMAC trial in sentinel lymph node-positive breast cancer. *Breast Cancer Res Treat* 2020;180:167–76.
- 24 de Boniface J, Frisell J, Andersson Y, *et al.* Survival and Axillary recurrence following sentinel node-positive breast cancer without completion axillary lymph node dissection: the randomized controlled SENOMAC trial. *BMC Cancer* 2017;17:379.
- 25 Sjöström M, Fyles A, Liu F-F, *et al.* Development and validation of a genomic profile for the omission of local adjuvant radiation in breast cancer. *J Clin Oncol* 2023;41:1533–40.
- 26 Murray Brunt A, Haviland JS, Wheatley DA, *et al.* Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. *Lancet* 2020;395:1613–26.
- 27 Group S. Riktlinjer för volymer och teknik vid strålbehandling av bröstcancer version 5, . 2022 Available: http://www.swebcg.se/wp-content/uploads/2022/04/Riktlinjer-f%C3%B6r-volymer-och-teknik-vid-br%C3%B6stcancer_Version-5.pdf
- 28 Adra J, Lundstedt D, Killander F, *et al.* Distribution of locoregional breast cancer recurrence in relation to postoperative radiation fields and biological subtypes. *Int J Radiat Oncol Biol Phys* 2019;105:285–95.

T-REX studien: Behövs strålbehandling mot närliggande lymfkörtlar för bröstcancerpatienter med en begränsad lymfkörtelspridning?

(Tailored Regional External beam radiotherapy in clinically node-negative breast cancer patients with 1-2 sentinel node macrometastases)

Information till forskningspersoner

Vi vill fråga dig om du vill delta i ett forskningsprojekt som kallas T-REX studien. I det här dokumentet får du information om projektet och om vad det innebär att delta.

Ditt deltagande är frivilligt och du kan när som helst välja att avbryta deltagandet. Om du väljer att inte delta eller vill avbryta ditt deltagande behöver du inte uppge varför, och det kommer inte heller att påverka din framtida vård eller behandling. Om du vill avbryta ditt deltagande ska du kontakta studieansvarig forskningssköterska vid din behandlande klinik.

Vad är det för ett projekt och varför vill ni att jag ska delta?

Projektet undersöker om de volymer som strålbehandlas efter bröstcancerkirurgi kan minskas för patienter som har en begränsad spridning till lymfkörtlarna. Tidigare studier visar att mindre strålbehandling ger lägre risk för biverkningar som smärta, svullnad och försämrad funktion i arm/skuldra. Dessutom minskas stråldosen till lunga och ev. hjärta och den risk för lungcancer och hjärtsjukdom som strålbehandling kan medföra på längre sikt.

Vid bröstcancerkirurgi genomförs oftast en sentinel node-biopsi, vilket innebär att man opererar ut en eller ett fåtal ”portvaktslymfkörtlar” för att se om bröstcanceren har spridit tumörceller till armhålan. Denna information styr val av efterbehandling (t.ex. strålbehandling, antihormonella läkemedel och cellgifter).

Om tumörceller hittas i sentinel node (portvaktslymfkörteln) ges i Sverige idag strålbehandling mot kvarvarande lymfkörtlar i armhålan, kring nyckelbenet och i vissa fall vid bröstbenet. Äldre studier har visat en viss överlevnadsvinst av sådan behandling, men med dagens förbättrade läkemedelsbehandling är det tveksamt om denna strålning fortfarande behövs. Moderna studier där man jämfört en grupp av patienter som genomgått kirurgi/strålbehandling mot armhålan lymfkörtlar med en grupp där man avstått denna behandling har inte visat någon skillnad i återfallsrisk, trots mindre behandling i den ena gruppen.

I T-REX studien undersöks om strålbehandling mot lymfkörtlarna kan avstås vid bröstcancer med en begränsad körtelspridning. Därigenom kommer strålbehandlingens biverkningar kunna minskas eller helt undvikas. Projektet planerar att inkludera 1350 patienter och kommer pågå vid flera kliniker i Sverige samt i Norge och Finland.

Forskningshuvudman är Skånes Universitetssjukhus, Region Skåne. Med forskningshuvudman menas den organisation som är ansvarig för projektet. Ansökan är godkänd av Etikprövningsmyndigheten, diarienummer för prövningen hos Etikprövningsmyndigheten är 2022-02178-01 och 2022-05093-02.

T-REX studien: Behövs strålbehandling mot närliggande lymfkörtlar för bröstcancerpatienter med en begränsad lymfkörtelspridning?

(Tailored Regional External beam radiotherapy in clinically node-negative breast cancer patients with 1-2 sentinel node macrometastases)

Hur går projektet till?

Att du tillfrågas om projektet beror på att din bortopererade sentinel node innehåller cancerceller, samt din tumör har «snällare» egenskaper (uttryck av östrogenreceptorn, men ej en annan faktor viktig för tumörutveckling kallad HER2). Om du deltar kommer du lottas till att antingen få standardbehandling (strålbehandling mot lymfkörtlar i armhålan, kring nyckelbenet och ev. kring bröstbenet) alternativt ingen strålbehandling mot lymfkörtlarna. Om bröstet opererats bort ges då ingen strålbehandling alls och efter bröstbevarande kirurgi ges strålbehandling enbart mot kvarvarande bröst.

Deltagande i projektet kommer inte påverka din läkemedelsbehandling, tid till start av strålbehandling eller den strålningsteknik som används. Uppföljning sker på din onkologiska eller kirurgiska klinik enligt deras vanliga rutiner.

Att avstå lymfkörtelbestrålning kan leda till minskade armproblem, minskad risk för biverkningar från hjärta och lunga och ökad livskvalitet. Inom projektet vill vi därför veta vilka besvär du upplever både inför och efter din behandling. Enkäter med frågor kring funktion i arm/hand/skuldra, välmående och livskvalitet kommer därför lämnas till dig vid studiestart samt 1, 3 och 5 år efter operationen. Dessa tar ca 10-15 minuter att fylla i. Deltagande är frivilligt, och du kan välja att avstå från enkäterna och ändå delta i huvudprojektet.

För de deltagare som ger sitt godkännande för analys av tumörvävnad kommer tumörens genuttryck att undersökas, för att se om denna analys bättre än dagens metoder kan förutsäga nyttan av strålbehandling. Detta kan i så fall användas för att förbättra och individanpassa strålbehandlingen för framtida patienter. Analysen görs hos ett företag i USA (Exact Sciences), till vilket vävnadsmaterial från den tumör som opererats bort skickas. Detta företag har expertkunskaper på undersökning av tumörers genuttryck och har deltagit i flera liknande internationella studier tidigare.

Möjliga följder och risker med att delta i projektet

Om du lottas till studiegruppen kommer du få mindre strålbehandling än dagens standard. Du får därmed också en mindre risk för biverkningar av strålbehandlingen.

Äldre studier har visat en skyddande effekt av strålning mot återfall i kvarvarande bröst/bröstkorgsvägg och lymfkörtlar, vilket hade kunnat innebära att mindre strålbehandling ökar återfallsrisken något. Idag används dock bättre och nyare bröstcancerläkemedel, vilket kraftigt har minskat risken för återfall. Nyare studier visar heller inte på någon riskökning med mindre kirurgi/strålning, vilket talar för att strålbehandlingen idag kan minskas för vissa tumörtyper och det är detta vi undersöker inom T-REX studien.

T-REX studien: Behövs strålbehandling mot närliggande lymfkörtlar för bröstcancerpatienter med en begränsad lymfkörtelspridning?

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Efter behandling kommer du följas vid din onkologiska eller kirurgiska klinik. Skulle det uppstå ett återfall i armhålan eller i bröstet/bröstkorgsväggen hanteras det enligt klinisk rutin, vilket kan innebära kirurgi och medicinsk behandling.

Vad händer med mina uppgifter?

Projektet kommer att samla in och registrera information om dig. Denna hanteras så att obehöriga inte kan ta del av den.

Ingår du i projektet registreras din information i en databas som hanteras och monitoreras av Kliniska Studier Sverige, Forum Söder, Region Skåne. Uppgifter om din tumör, behandling, resultat från operation, diagnostik och återbesök pseudonymiseras, dvs du som deltagare får ett «studie-ID» så att ditt personnummer eller ditt namn inte finns i databasen. Nyckeln som kopplar ditt personnummer och ditt namn till studie-ID finns på det sjukhus där du inkluderats i projektet, samt hos studieansvariga inom Region Skåne. För att garantera hög kvalitet på studiegenomförande kommer oberoende granskare (monitorer) ta del av din information och kontrollera uppgifter i din journal. Tillgång till dina journaluppgifter kommer behövas tills projektet är avslutat, vilket är 25 år efter sista studiepatienten inkluderats. All hantering av information sker i enlighet med EU:s dataskyddsförordning (General Data Protection Regulation, GDPR). Information kommer även inhämtas från nationella register, t ex det nationella kvalitetsregistret för bröstcancer, försäkringskassans register om sjukskrivning, socialstyrelsens patientregister som registrerar vårdkonsumtion och register avseende cancersjukdom och överlevnad.

För att säkerställa att din strålbehandling givits i enlighet med studieprotokollet, och att uppgifter om den har registrerats och lagrats korrekt, lämnas personuppgifter ut från ditt behandlande sjukhus till studieansvariga inom Region Skåne. Oberoende experter tar sedan del av röntgenbilder som visar strålbehandlingsplanen samt tillhörande behandlingssammanfattning. Även dessa experter är ålagda ansvar om sekretess.

Ansvarig för dina personuppgifter är Region Skåne och den region i vilken du behandlas. Enligt EU:s dataskyddsförordning har du rätt att kostnadsfritt få ta del av de uppgifter om dig som hanteras i projektet, och vid behov få eventuella fel rättade. Du kan också begära att uppgifter om dig raderas samt att behandlingen av dina personuppgifter begränsas. Rätten till radering och till begränsning av behandling av personuppgifter gäller dock inte när uppgifterna är nödvändiga för den aktuella forskningen. Om du vill ta del av uppgifterna ska du kontakta din lokala forskningssköterska. Dataskyddsombud nås på region@skane.se eller 044-3093000, eller för det lokala dataskyddsombudet på _____.

Om du är missnöjd med hur dina personuppgifter behandlas har du rätt att ge in klagomål till Integritetsskyddsmyndigheten, som är tillsynsmyndighet.

T-REX studien: Behövs strålbehandling mot närliggande lymfkörtlar för bröstcancerpatienter med en begränsad lymfkörtelspridning?

(Tailored Regional External beam radiotherapy in clinically node-negative breast cancer patients with 1-2 sentinel node macrometastases)

Vad händer med mina prover?

För de deltagare som godkänner analys av vävnadsprover skickas en vävnadsbit från den tumör som tagits bort under operationen till Västra Götalandsregionen, Biobank Väst, IVO-nummer 890. En provsamlings kallad T-REX kommer sättas upp vid verksamheten för Onkologi, Sahlgrenska Universitetssjukhuset, Västra Götalandsregionen. I provsamlings kommer en bit av vävnaden förvaras för analyser avseende tumörens biologi i förhållande till återfallsrisk och behandlingseffekt. En mindre mängd av vävnaden kommer även skickas för analys från Biobank Väst till ett företag i USA (Exact Sciences). Resten av vävnadsbiten skickas tillbaka till din hemmaklinik. Samtliga ovan nämnda prov kommer att vara kodade (pseudonymiserade) som beskrivet ovan. Vävnad kan också komma att samlas in från eventuella bröstcanceråterfall.

Du har rätt att utan förklaring säga nej till att proverna sparas. Om du samtycker till att proverna sparas har du rätt att senare och utan förklaring ångra det samtycket. Dina prover kommer i så fall att kastas eller avidentifieras. Om du vill ångra ett samtycke ska du kontakta din lokala forskningssköterska.

Analys av dina vävnadsprover syftar till att förbättra och individualisera strålbehandlingen efter tumörens biologi för framtida patienter. Proverna hanteras enligt Svensk Biobankslag (2002:297) och får endast användas på det sätt du samtyckt till. Vill du inte att dina prover ska vara tillgängliga för analyser inom projektet skriver du ej under avsnittet avseende samtycke för analys av tumörvävnad (sista sidan i patientinformationen).

Hur får jag information om resultatet av projektet?

Resultaten från projektet kommer publiceras i vetenskapliga tidskrifter och vid vetenskapliga kongresser. Detta sker på gruppnivå utan att resultaten kan kopplas till dig som individ.

Försäkring och ersättning

Inom projektet gäller patientförsäkringen som annars inom vården. Man får ingen ekonomisk ersättning för deltagande.

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Ansvariga för projektet

Docent, specialistläkare Sara Alkner, Verksamhetsområde onkologi, hematologi och strålningsfysik, Skånes Universitetssjukhus samt Avdelningen för onkologi, Lunds Universitet.

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Docent, överläkare Jana de Boniface, Bröstenheten, Capio St Göran's sjukhus samt Avdelningen för molekylär medicin och kirurgi, Karolinska Institutet, Stockholm.

Professor, överläkare Per Karlsson, Onkologiska kliniken, Sahlgrenska Universitetssjukhus samt Avdelningen för onkologi, Göteborgs Universitet, Göteborg.

Överläkare, PhD Dan Lundstedt, Onkologiska kliniken, Sahlgrenska Universitetssjukhus samt Avdelningen för onkologi, Göteborgs Universitet, Göteborg.

Professor, överläkare Lisa Rydén, Kirurgiska Kliniken, Skånes Universitetssjukhus samt Avdelningen för onkologi, Lunds Universitet.

Lokalt ansvariga kontaktpersoner

Ansvarig forskare: _____

Ansvarig forskningssköterska: _____

T-REX studien: Behövs strålbehandling mot närliggande lymfkörtlar för bröstcancerpatienter med en begränsad lymfkörtelspridning?

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Samtycke till att delta i projektet

Jag har fått muntlig och/eller skriftlig information om T-REX studien och har haft möjlighet att ställa frågor. Jag får behålla den skriftliga informationen.

Jag vet att mitt deltagande i projektet är frivilligt samt att jag när som helst och utan förklaring kan avbryta mitt deltagande. Jag samtycker till att oberoende granskare får ta del till mina journaluppgifter för att verifiera data och säkerställa kvalitet samt att extern oberoende granskning av strålbehandlingens kvalitet får ske på beskrivet sätt, och till att mina personuppgifter får behandlas enligt den information jag har fått

- Jag samtycker till att delta i projektet «Minskad strålbehandling mot närliggande lymfkörtlar till bröstcancerpatienter med låg återfallsrisk: T-REX studien.»

.....
Patientens underskrift

.....
Personnummer

.....
Namnförtydligande

.....
Datum

Samtycke till analys av tumörvävnad

Jag har fått information om att de prover jag lämnar kommer användas för analyser av tumörbiologi i förhållande till återfallsrisk och nytta av återfallsförebyggande behandling. Jag har även fått information om att de prover jag lämnar kan bli aktuella för framtida forskning som inte är beskriven i informationen till mig som forskningsperson. I det fall mina prover ska användas i framtida forskning kommer Etikprövningsmyndigheten göra en prövning av det nya projektet och i sin prövning avgöra om jag ska tillfrågas på nytt.

- Jag samtycker till att vävnad från operationen och eventuella bröstcanceråterfall sänds till Biobank Väst sparas i en för studien avsedd provsamling och analyseras enligt beskrivningen i patientinformationen.
- Jag samtycker till att mina prover får sparas för framtida forskning.

.....
Patientens underskrift

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Datum

Jag har förklarat projektets upplägg och syfte för ovanstående patient och har noggrant informerat om målsättning och eventuella risker med projektet, samt verifierar att patienten läst och erhållit informationsbladet.

.....
Läkarens underskrift

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Datum

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Namnförtydligande