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Patient preferences regarding intraoperative versus external beam radiotherapy for early breast cancer and the impact of socio-demographic factors

Saskia Spaich[1] · Sophie Krickeberg[1] · Svetlana Hetjens[3] · Frederik Wenz[4] · Axel Gerhardt[1,2] · Marc Sütterlin[1]

Abstract

Purpose Patient comfort and preference have steadily gained attention in radio-oncologic treatment of breast cancer. Therefore, the purpose of this investigation was to further explore patient preferences in choosing between intraoperative radiotherapy (IORT) and external beam radiotherapy (EBRT).

Methods We prospectively analysed data of 101 women, who were candidates for breast-conserving surgery with adjuvant radiotherapy. A two-part video was shown to patients: an educational section about EBRT/IORT, followed by a preference elicitation section focusing on additional accepted risk (AAR) of recurrence after either treatment. Furthermore, participants completed a questionnaire to identify factors that influence patient preference of radiation modality.

Results The data demonstrate that 42.5% of patients would accept additional risk of recurrence for IORT versus 9% AAR for EBRT, while 48.5% of patients would not accept any additional risk, yet would choose IORT over EBRT if risks of recurrence were equivalent. When combining patient preferences and the results from the questionnaire, no single socio-economic/-demographic factor was found to significantly correlate with AAR of IORT.

Conclusion Our study confirms the existence of subgroups of breast cancer patients who would accept an additional risk of recurrence associated with choice of radiation modality to receive a single dose of IORT as adjuvant radiotherapy for breast cancer instead of EBRT over several weeks; yet our data fail to identify a single factor significantly associated with these patient preferences and, therefore, helpful for individualised decision-making processes.

Keywords Intraoperative radiotherapy (IORT) · Breast cancer · Breast-conserving surgery · Patient preference · External beam whole breast radiotherapy (EBRT) · Shared decision-making

Axel Gerhardt and Marc Sütterlin authors contributed equally.

✉ Saskia Spaich
saskia.spaich@umm.de

1 Department of Obstetrics and Gynaecology, University Medical Centre Mannheim, Heidelberg University, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany

2 Department of Gynaecology and Obstetrics, St. Hedwig Klinik, Mannheim, Germany

3 Department of Medical Statistics and Biomathematics, University Medical Centre Mannheim, Heidelberg University, Mannheim, Germany

4 Department of Radiation Oncology, University Medical Centre Mannheim, Heidelberg University, Mannheim, Germany

List of Abbreviations

|	
AAR	Additional accepted risk
BCS	Breast-conserving surgery
EBRT	External beam whole breast radiotherapy
IORT	Intraoperative radiotherapy

Introduction

The incidence of breast cancer is steadily increasing. Accounting for 23% of cancers in women, breast cancer is the most common malignant neoplasm in women and—despite significant advances in therapy—remains a frequent cause of death [1, 2]. Modern treatment of breast cancer is characterised by a multimodal therapeutic approach.

Early breast cancer is usually treated with breast-conserving surgery (BCS) followed by radiation therapy [2]. In this regard, external beam whole breast radiotherapy
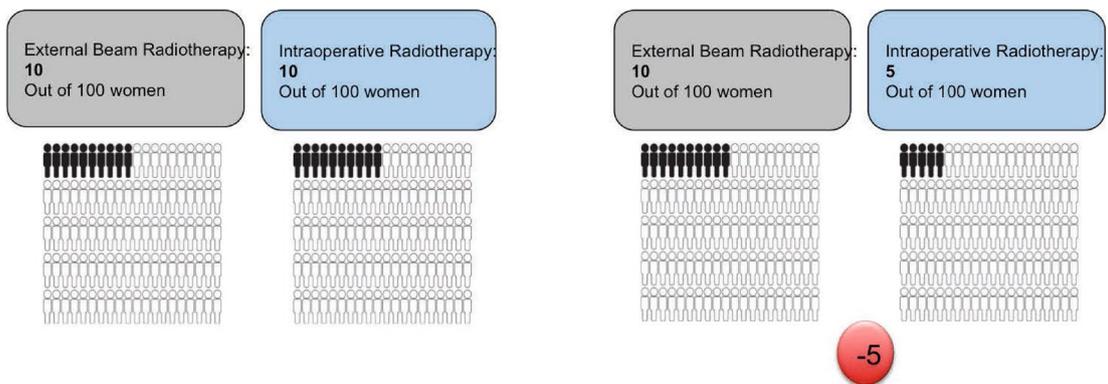
A Expected frequency of side effects

Side effects	IORT [%]	EBRT [%]
Induration	17	18
Erythema	6	18
Breast seroma	2	8
Skin retraction	41	26
Open wound	2	0
Axillary seroma	2	4
Color change of skin	6	8
Pain	21	16

B Patient-perceived importance of treatment options
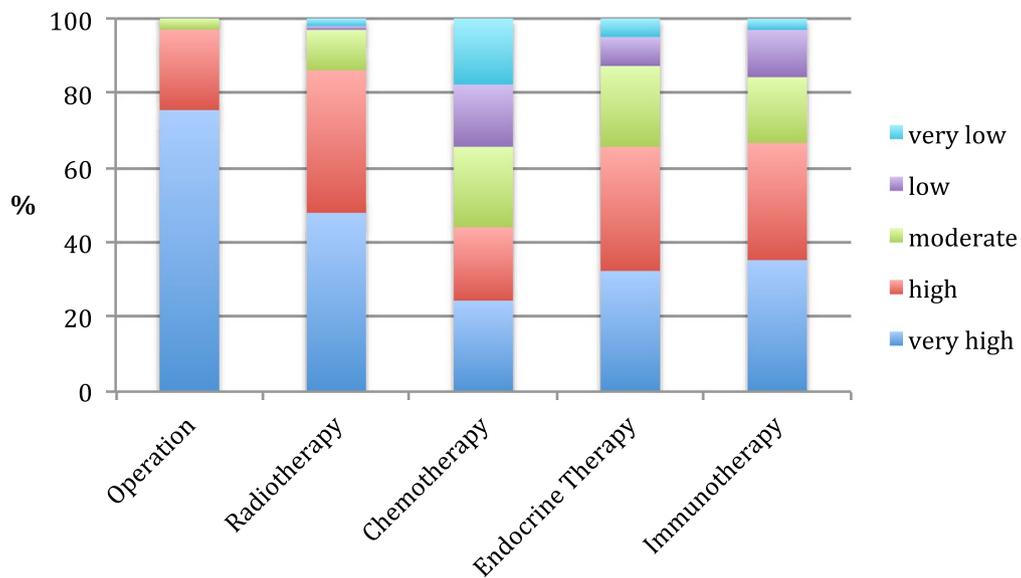
C Hypothetical 10 year risk of recurrence

◀**Fig. 1** **a** Comparison of expected frequency of side effects in IORT vs. EBRT (in % of patients treated); **b** Subjective importance of treatment options as perceived by breast cancer patients. More than 80% of patients attribute high or very high importance to surgery and radiotherapy. **c** Exemplary illustration as presented to patients as part of the trade-off technique of questioning. The baseline presentation (left side) stated a hypothetical risk of 10-year local recurrence of 10% for both EBRT and IORT, thus denominating parity of options. In the following (right side), hypothetical risk of recurrence was left unaltered for EBRT at 10%/10 years, while risk of recurrence was modified in the IORT group (in this case 5%/10 years)

(EBRT) has long been the standard of care in breast cancer treatment. Nowadays, multiple radiation modalities exist, differing by duration of treatment, side effects, cosmetics, convenience and costs [3, 4]. Specifically, there are different techniques including the EBRT on the one hand, and intraoperative radiotherapy (IORT) with electrons or low-energy X-rays on the other hand [5–7]. While EBRT generally takes 3–6 weeks, IORT is delivered only once at the time of BCS, i.e., during surgery.

Several studies demonstrate that efficacy and safety of IORT are generally not inferior to EBRT in low-risk-patient cohorts [2, 6, 8]. Intriguingly, IORT may not only offer advantages in regard to geographic and temporal miss of residual tumour tissue but also may even be superior in terms of patient comfort [2, 6, 7, 9].

While the TARGIT-A trial—designed as a non-inferiority study—demonstrated that additional risk of recurrence for IORT (in comparison to EBRT) did not exceed a non-inferiority margin of 2.5%, the general question remains whether patients would be willing to take an additional risk of recurrence with IORT [6].

In light of this non-inferiority of IORT, aspects of patient comfort and preference are gaining more attention. The concept of shared decision-making has been well established in (breast) cancer treatment for years. Risk of recurrence and overall survival have been elucidated as key parameters that guide patient preferences [10]. As part of the effort to optimise and integrate future treatment strategies into individualised therapies, it will be paramount to identify socio-economic and -demographic factors as well as mindsets that drive this decision-making process in special subgroups of patients.

As data on patient preferences regarding EBRT and IORT are limited [10], the purpose of this investigation was to further explore and quantify patient preferences by prospectively presenting different hypothetical risk scenarios comparing EBRT and IORT. Thereby, we attempted to identify and stratify different subgroups of patients, whose therapeutic choices could potentially be influenced by socio-demographic factors, lifestyle and general mindset.

Methods

Over a time period of 26 months, a total of 101 consecutive patients with newly diagnosed breast cancer, who were current candidates for breast-conserving surgery with adjuvant radiotherapy at the University Medical Centre Mannheim, were included in the study. All patients provided informed consent. Ethical approval was obtained through the Ethics Committee II of Heidelberg University, Medical Faculty Mannheim (2013-591N-MA).

Study protocol

The study was conducted after patients were informed about their diagnosis, but before potential treatment plans and modalities had been discussed, to avoid any confounding influence on patient choices. Patients were informed about the existence of national and international guidelines for breast cancer treatment as well as the tumour board concept to optimise individualised therapy.

A two-part video was shown to patients: an introductory educational section about EBRT and IORT, and a preference elicitation section regarding the hypothetical risk of recurrence for either treatment. Furthermore, the women obtained a questionnaire about medical and personal history and their environment.

The introductory section offered thorough information on IORT and EBRT in terms of procedures and possible side effects. The method used was predicated on that used by "decision boards" [10, 11]. Specifically, EBRT was presented as a regimen of 10–15 min of radiation daily, 5 days per week lasting 5–6.5 weeks, while IORT was presented as a one-time radiation administered during surgery (duration 25–40 min). Patients were also briefed on a potential escalation strategy in case of high risk circumstances (grading, size, etc.), involving IORT followed by an abbreviated regimen of EBRT.

Subsequently, patients were provided with a tabular illustration of potential side effects of both treatment options along with respective frequencies (Fig. 1a).

Following the educational section, patients were asked about individual treatment preferences. Specifically, they were requested to base their decision on potential risk of recurrence. For this assessment a trade-off technique was used, which allowed us to quantify the additional risk of recurrence that patients would be willing to accept with each treatment modality. These trade-off techniques studies offer a valuable tool for the process of shared decision-making in the clinical setting as well as assessment of patient preferences to guide decisions in health economy [10–12].

Hypothetical risk of local recurrence within 10 years was illustrated for both treatment groups (EBRT and IORT) by iconic graphs that featured shaded figures as being affected, while blank figures represented healthy individuals per 100 patients treated with the respective treatment option (Fig. 1c). This type of illustration is well established for risk assessment and communication [13, 14]. Accepted additional risk as the primary endpoint was defined as the cut-off point when patients decided that they would no longer accept an increment in risk of local recurrence for the given treatment modality.

The baseline presentation stated a hypothetical risk of 10-year local recurrence of 10% for both EBRT and IORT, thus denominating parity of options. In the following, hypothetical risk of recurrence was left unaltered for EBRT at 10%/10 years, while risk of recurrence was modified in the IORT group. With each scenario, risk of recurrence for IORT was lowered by 1% until the patient decided that the alteration in risk would cause him to switch therapeutic modalities. When this algorithm had been completed, the patient was confronted with scenarios in which the hypothetical baseline risk of 10% was successively incremented by 1% for IORT with each step until it reached 20%, while the risk of recurrence in the EBRT group was again left unaltered at 10%/10 years. Again, the scenario that caused a patient to switch preferences was noted, denominating each patient's AAR in regard to IORT.

Questionnaire on socio-economic/-demographic factors and mindset

After completing the preference elicitation section, the participants received a questionnaire about their personal, professional and medical history as well as their general mindset. Specifically, women were asked to provide details about their age, distance to treatment facility, relationship status, level of education and current/past employment. In detail, questions covered whether they were working full time or part time, if they were reliant on their own income and if they had to take care of somebody else. Finally, they were interrogated about their mindset in terms of personal needs and expectations concerning their individual treatment, what they perceived to be the most important aspect of their treatment and their desired individual relationship to the treating medical professionals. The freeware "LimeSurvey" was used for data collection with this questionnaire (LimeSurvey V2.00+/http://www.limesurvey.org).

Multivariate analyses of determinants of AAR

Finally, we sought to determine if we could identify socio-economic and -demographic factors as well as general attitudes that had influenced the AAR in our cohort. Therefore,

a multivariate regression model with forward selection ($\alpha = 5\%$) was implemented with AAR being the dependent variable. Items from the questionnaire on general mindset of patients as well as socio-economic and -demographic factors were considered independent variables.

Statistical assessment was performed using SAS software (SAS Institute, www.sas.com) in cooperation with the Department of Statistics and Bioinformatics of the Medical Faculty Mannheim, Heidelberg University.

Results

Our study analysed data of 101 consecutive patients. Age of the 101 included women ranged from 29 to 89 years (mean = 64 years), with the majority of women being between age 50 and 69. All patients had previously been informed about the diagnosis of breast cancer without metastasis, whereas they had not yet been in contact with a radiation oncologist or oncologist before recruitment and conduction of our study.

When patients were asked to judge the importance of respective treatment modalities currently established in breast cancer therapy, nearly all women perceived surgery as critical for success of treatment (97%). However, most of our patients (86%) also attributed great importance to radiation therapy as part of their treatment (Fig. 1b).

Comparison of treatment modalities and AAR

The majority of participants (91%) would choose IORT over EBRT if risk of recurrence with IORT was equal to that of standard EBRT; only one woman refused IORT completely. Forty-nine women (48.5%) accepted IORT at no additional risk, while 43 patients (42.5%) would choose IORT even with some additional risk of having a local recurrence within 10 years (Fig. 2a and b). Mean additional accepted risk for IORT was 1.99%.

Interestingly, 15 patients (15%) preferred IORT even if additional risk of local recurrence would double with this treatment option (10% EBRT versus 20% IORT)—Fig. 2a.

Lifestyle and mindset, socio-demographic and socio-economic factors

Detailed patient characteristics and socio-demographic factors as well as individual treatment priorities are presented in Table 1.

In terms of marital status, the majority of women were in a partnership, either married (52%) or in a stable relationship (9%), 19% of patients were widowed and the rest were single or divorced (21%).

A

B
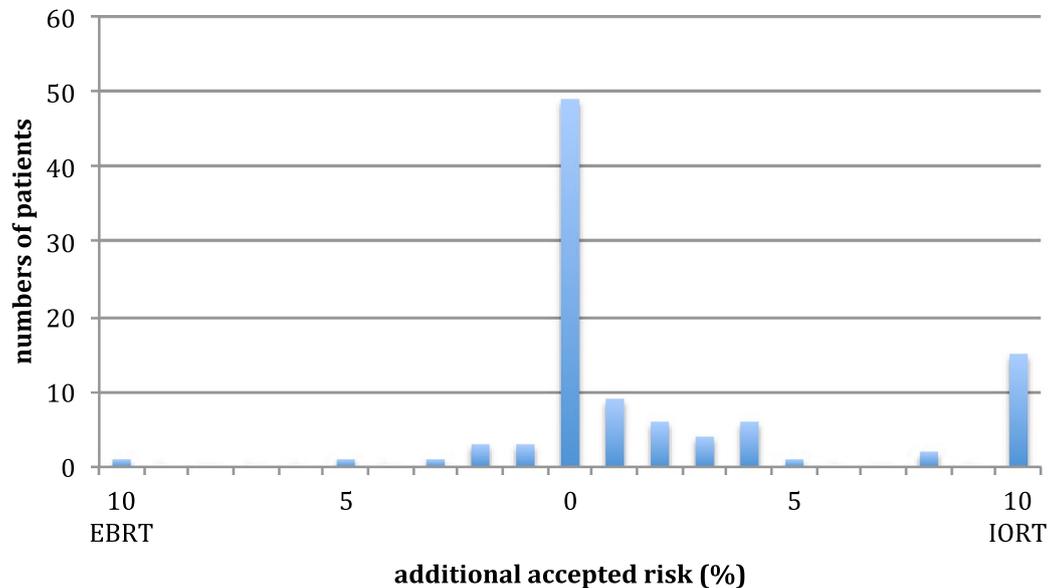
Mean additional accepted risk with IORT vs. EBRT	1,99%
patients with preference for EBRT with additional risk	9%
patients with preference for IORT with additional risk	42.5%
patients with preference for IORT at equivalent risk	48.5%
patients with preference for EBRT at equivalent risk	0%

Fig. 2 a Frequency distribution of patients' additional accepted risk (AAR) for respective treatment modalities (left side favouring EBRT, right side favouring IORT). **b** Table illustrating the share of patients in favour of each treatment modality at additional or equivalent risk. Mean additional risk with IORT vs. EBRT is 1.99%

When asked about distance as a potential determinant of treatment choices, 32% of women stated that it took 15–30 min time commuting to the radiation facility, while 23% of patients had to travel more than 30 min. The majority of patients had low or mid education. In this regard, 56% of women had received non-academic job training and only 18% of women had a college graduate degree.

Most of the women (61%) were retired at the time of questioning, while only 17% of women were working full time. Congruently, the majority of participants (63%) were not reliant on their own income. Only 11% of the women had to take care of somebody else in the family at the time of questioning. When it came to choosing the radiation facility, 32% of the patients voiced a pivotal preference for a specialised Breast Cancer Centre, whereas for 31% of women, recommendation by a friend was the most important determinant in choosing a treatment facility. Other patients' preferences were guided primarily by short distance to the respective treatment centre (12%), special treatment options (15%) such as IORT or a possible participation in current trials.

When asked about the most important issue for their treatment, long-term overall survival was top priority for the majority of patients (57%), followed by good tolerance of respective treatment (26%) and a short treatment period (11%).

Patients were split in regard to preferring a stable one-to-one relationship to their respective physician (50%) or whether a team of specialists should attend to them and their treatment (50%).

Correlation/association of individual patient data and treatment preference

The primary aim of this study was to determine whether willingness to accept an additional risk of recurrence was

Table 1 Patient characteristics and results of the questionnaire on socio-demographic and socio-economic factors

| Characteristics	n (abs.)
Age	
<50 years	9
50–69 years	56
>69 years	36
Marital status	
Single	9
Stable relationship	9
Married	52
Divorced	12
Widowed	19
Travel time	
<15 min	46
15–30 min	32
>30 min	23
Schooling	
Low	39
Mid	30
High	29
Other	3
Professional education	
Low	13
Mid	62
High	18
Other	8
Employment	
Employed	32
Selfemployed	5
Pensioner	62
Unemployed	2
Working status	
Full time	19
Part time	17
Other	65
Dependence on salary	
Yes	29
No (w/high standard of living)	9
No (w/normal standard of living)	63
Status as primary caregiver (for)	
No	90
Kids	5
Parents	3
Other	3
Key logistic requirement for treatment	
Short distance	12
Recommendation by confidant	31
University hospital	11
Specialised breast cancer centre	32
Key determinant of treatment success	
Long overall survival	58

Table 1 (continued)

Characteristics	n (abs.)
Good tolerance	25
Short treatment	18
Relationship to treating physician	
Team of experts	51
Single person of trust	50

associated with any of the items assessed in the questionnaire in regard to social, financial and personal aspects of the patients' lives. However, when statistical analyses were performed by implementation of multivariate regression, no significant association was observed for any single parameter (Fig. 3)—i.e. age at diagnosis, distance to treatment facility, relationship status, level of education, current job as well as standard weekly hours on the job did not have a significant influence on the patients decision for either treatment modality when tested in a multivariate regression model. Neither did patients' dependence on salary nor the need to take care of family members affects the additional accepted risk and, thus, the choice of treatment. Furthermore, general mindset and attitudes towards treatment such as personal priorities and important requirements to be met by the centre or the medical professionals could not be identified as critical parameters that would help in prediction of AAR in our cohort of patients.

Discussion

Breast cancer treatment has seen an impressive evolution as therapeutic options and regimens have been augmented by the addition and combination of new drugs on the one hand, and fascinating developments in radiotherapy on the other hand. In regard to the latter, several studies could demonstrate that efficacy and safety of IORT are not inferior to conventional treatment, establishing this modality as a beneficial alternative for treatment in breast cancer patients [6, 15–18]. Furthermore, cosmetic results do not seem to differ—even after administration of neoadjuvant chemotherapy [19].

Implementation of a valid shared decision-making process appears mandatory to determine individualised therapeutic options for patients. From an economic perspective, this patient-centred approach might also confer significant benefits, as estimations attribute about half of healthcare costs to decisions primarily driven by doctors and hospital supply rather than patient need and demand [20, 21]. Therefore, focusing on patient preferences and elucidating reasons for individual choices in regard to certain therapies may strengthen economical yet effective approaches, while
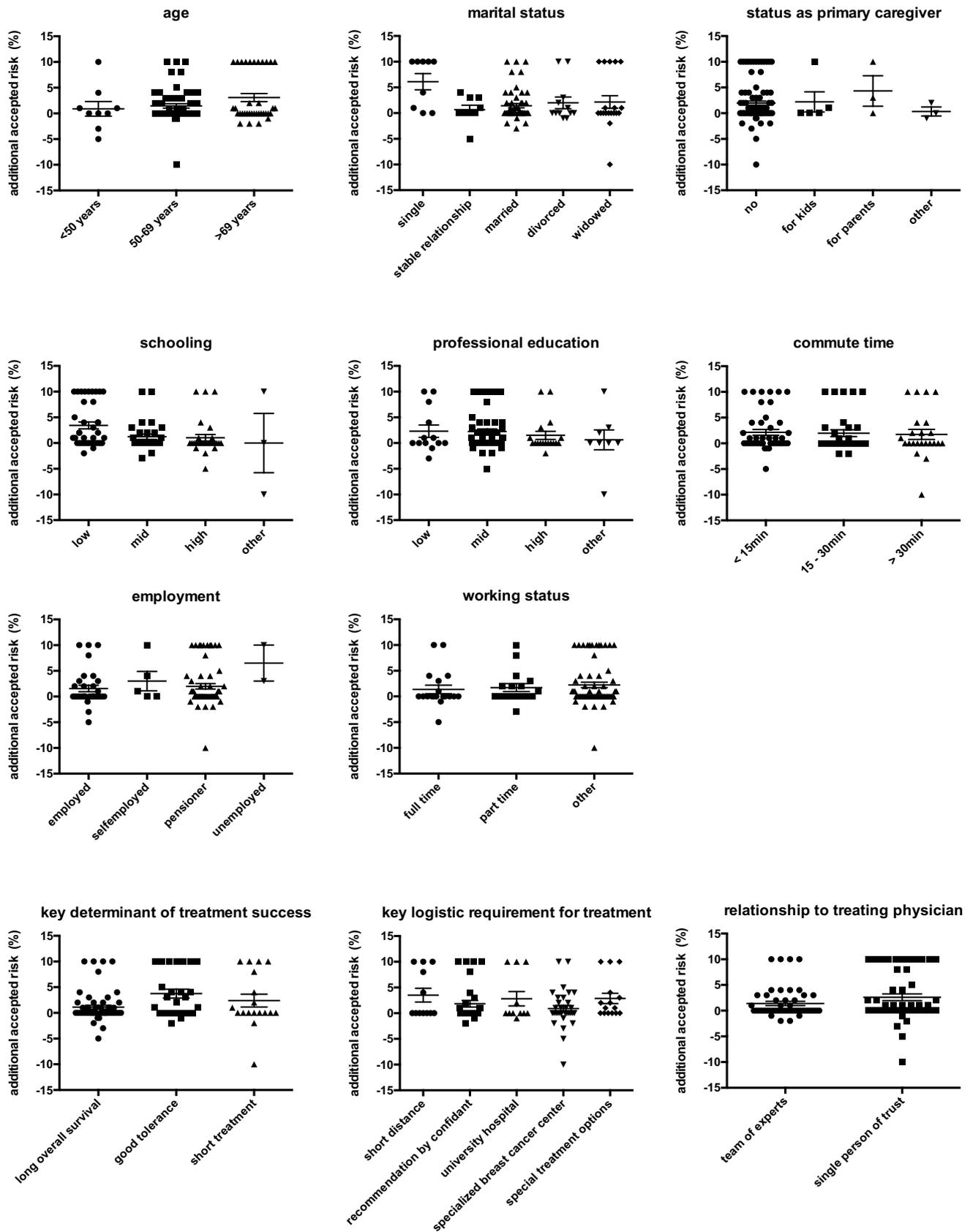
Fig. 3 Illustration of socio-demographic factors and their impact on patient preference regarding additional accepted risk for IORT vs. EBRT (positive values favour IORT, while negative values favour EBRT). All comparisons do not reach statistical significance ($p > 0.05$)

helping us in providing best care for each patient tailored to his/her individual situation and mindset.

As trade-off techniques and other questionnaires have been successfully used to determine patient preferences in breast cancer radiotherapy [10, 11], our study aimed to further characterise these priorities and gain insight into socio-demographic and socio-economic factors that drive these decisions and may cause a patient to sway to a more conservative or innovative treatment pathway/approach.

The results of this study show that almost half of the patients (43%) would prefer IORT even at some increased risk of local recurrence, which is in congruence with data from a recent study by Alvarado et al. [10], who could also show that patients generally tended to favour IORT over EBRT in questionnaires using trade-off techniques. The majority of women in our study (91%) preferred the IORT option at equivalent local recurrence risk. The mean additional accepted risk for IORT was 1.99% in this study and 3.2% in the study of Alvarado and colleagues. However, it is important to note, that in a study asking the question in retrospect, the readiness to accept an additional risk is very likely to be higher, as the procedure associated with a risk lies in the past and the risk itself may not be perceived as a real potential threat anymore.

Interestingly, in both studies, 9% of patients would favour EBRT over IORT, even if recurrence risk would be elevated with EBRT, suggesting that about one in ten patients in both study populations preferred a conservative pathway with a longstanding treatment modality, even if a more modern approach might potentially reduce their morbidity or mortality. On the other hand, most patients (>90%) demonstrate a positive attitude to new therapeutic approaches that are perceived as non-inferior (as is general practice for initial approval of new therapies). Moreover, both our study and the study of Alvarado and colleagues show that a relevant fraction of breast cancer patients (43% and 64%, respectively) states that they are open minded towards innovative treatment strategies that might even carry some increased risk of recurrence. The above-mentioned difference found in both studies (43% vs. 64%) is probably founded in differences in study recruitment and timing, as our study was conducted before any treatment had taken place, whereas patients in the other study could be included even if radiation therapy had already been applied. In fact, 75% of patients had already completed their radiation therapy in the past in Alvarado's cohort [10]. This post hoc decision-making in terms of AAR might imply a serious bias as retrospective questioning probably led to higher risk propensity as opposed to prospective confrontation of patients with AAR.

Yet, our prospective evaluation validated many aspects from this retrospective approach in regard to the general mindset of breast cancer patients.

The previously cited combination of open-mindedness and willingness to accept an additional risk is also reflected in patients' priorities regarding overall treatment motifs, where—congruent with other studies [22–24]—only about two thirds of patients stated that long overall survival was most critical for them, while the other third of women indicated that the most relevant aspect for their treatment was either a short treatment duration or good tolerability of therapy. Nevertheless, our study could not demonstrate a significant correlation between short treatment duration as key issue and willingness to accept an additional risk with IORT alone.

In regard to the aspect of proximity to the treatment facility, we could not establish distance to treatment facility as a relevant factor for patient preferences in our data. This is in contrast to other studies of patient preferences that have shown a higher rate of mastectomy and a lower rate of adjuvant radiation with increasing distance to the radiation facility [25–28].

Of note, both our study and Alvarado's study identified a fraction of about 10% of patients who would be willing to subject themselves to IORT even if risk of recurrence doubled with this treatment modality as compared with standard EBRT. In an attempt to optimise patient-centred and individualised therapy, future research will have to dissect the factors that drive these opposing preferences and decisions. Importantly, the question will have to be addressed whether this willingness to take significant risks is a truly deliberate and voluntary decision by sufficiently educated patients or whether deficits in our healthcare system and individual hardships are truly responsible for these decisions. Our data suggest that patient motifs cannot be attributed to a lack of financial means, familial status or necessity to care for another individual (Fig. 3). However, a limitation of our study concerns the fact that our patient population was rather old, so that the majority had already retired and was not dependent on regular salary. Although we did not find evidence that age per se would influence AAR from radiotherapy, a note of caution seems warranted in this regard. Future research should gain more insight into younger patients' motivations and decisions, especially a cohort in which financial or social dependence of patients' relatives (especially children) may constitute an additional burden when evaluating individual therapeutic options. Our study does not provide adequate numbers in this subgroup of patients, as only about 10% of patients indicated that they had to take care of somebody else during their therapy.

As already exemplified above, none of the analysed individual factors alone drove patient preference towards one of the offered therapies (Fig. 3). However, it seems reasonable that studies in larger patient cohorts may identify combinations of social factors that do indeed guide individual patient

preferences and may, therefore, be helpful in optimising patient-centred approaches in the future.

Study limitations

The patient cohort analysed in this study was rather old (mean age = 64 years) and was neither dependent on financial regard nor did the majority have to provide for someone else, which might limit the significance of our findings for younger breast cancer patients. Furthermore, inherent to the study design, which set the (theoretical) baseline risk of recurrence to 10% as the benchmark, results might be different if baseline risk of recurrence was communicated to be significantly lower or higher depending on cancer entity and tumour stage. Therefore, this should be kept in mind, when conclusions from our findings are generalised for individual stages or other tumour entities.

While more than 100 patients were included in our study, a larger patient cohort would be helpful to dissect patterns and detect significant combinations of factors that drive patient preferences.

Conclusion

Our study on patient preferences regarding IORT vs. EBRT prospectively validates the existence of subgroups of patients that favour one treatment modality over the other despite significant additional risk of recurrence that might be associated with this choice. While about 10% of patients would choose EBRT even with an additional risk, nearly half of the patients would be willing to accept an additional risk of recurrence with IORT; if risk of recurrence was considered equal, patients favoured IORT.

To improve shared decision-making and individualised approaches in breast cancer therapy, it appears paramount to identify factors that drive patient preferences and to thoroughly characterise respective subgroups. However, our data on mindset, socio-economics and -demographics of breast cancer patients derived from a standardised questionnaire did not yield a single factor that correlates significantly with patient preference and AAR of each radiation modality.

Compliance with ethical standards

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