Evaluation of Patient Experience From Participation in a Randomised Trial.

Collins P[1,2], Khitab N[3,4], Pitsinis V[3,4], Benson JR[5,6].

[1]University of Cambridge, Cambridge [2]Clinical School, Cambridge UK, [3]Department of Breast Surgery, NHS Tayside, Dundee, UK, [4]University of Dundee, Dundee, UK [5]Cambridge Breast Unit, Addenbrooke's Hospital, Cambridge, [6]School of Medicine, Anglia Ruskin University, Cambridge and Chelmsford, UK

Abstract

Background: There are persistent barriers to recruitment of patients into surgical trials, especially those involving the process of randomization whereby there is uncertainty about allocation to an experimental intervention or standard treatment. A key challenge to recruitment relates to discrepant surgeon and patient preferences with lack of equipoise and a belief that outcomes for treatment options may differ in a predictable manner[1]. Trials involving novel methodology with limited data on efficacy compound these problems of recruitment. Minimal research has been undertaken on the process of randomization from a patient's perspective and how this removes an element of management choice with a perceived obligation to accept the allocated treatment and not withdraw from the trial after randomization. This study aimed to explore patient experience from participation in a randomised trial evaluating fluorescent navigation with indocyanine green (ICG) for sentinel node localization in early breast cancer[2].

Methods: A questionnaire was issued retrospectively to all trial patients (n=100) with key themes that explored motivation for trial participation, attitudes to randomization, adequacy of information provision and concerns about standard tracer agents. Almost half (45%) of patients responded with data quantified using a 10 point Likert scale (strongly agree [1], strongly disagree [10]. A one-sample T-test determined significance of deviation from the hypothesized neutral value of six. A mixed-methods approach provided holistic assessment of patients' experience with open-ended questions generating qualitative data for context. Employing a comprehensive post-study analysis, several positive messages were identified from this INFLUENCE trial that might inform the design and conduct of future surgical trials.

Results: A principle motivation for trial participation was a desire to help future patients (1.22; p<0.001). Patients appeared comfortable with random allocation to treatment groups (2.32; p<0.001) and were unconcerned about any potential negative impact from being part of the experimental arm (7.5; p<0.01). Pre-trial information was deemed accessible and comprehensive (1.93; p<0.001) and patients had sufficient time to process this before making any final decision on trial participation (1.75; p<0.001). Although patients were unconcerned about radioactive tracer usage (8.05; p<-.001), avoiding exposure to a source of radioactivity was considered an advantage of ICG alone for detection of sentinel nodes (3.67; p<0.001).

Conclusion: Results of this questionnaire are reassuring and confirm that any barriers to trial participation are not primarily related to concerns about the randomization process or allocation to an experimental treatment arm. Furthermore, this data suggests that any pre-existing concerns can be mitigated through effective pre-trial engagement and communication with the research team. A strong sense of altruism prevails amongst patients and highlights the importance of emphasizing the benefits of clinical research to prospective trial participants. Optimal and well-written pre-trial information is essential and patients should be allowed adequate time to process this information and reflect upon trial participation. Well-designed consent processes will positively influence enrolment along with transparent dialogue and trust in the healthcare professionals conducting the study.

Introduction

There are persistent barriers to recruitment of patients into surgical trials, especially those involving the process of randomization whereby there is uncertainty about allocation to an experimental intervention or standard treatment. A key challenge to recruitment relates to discrepant surgeon and patient preferences with lack of equipoise and a belief that outcomes for treatment options may differ in a predictable manner[1]. Trials involving novel methodology with limited data on efficacy compound these problems of recruitment. Minimal research has been undertaken on the process of randomization from a patient's perspective and how this removes an element of management choice with a perceived obligation to accept the allocated treatment and not withdraw from the trial after randomisation.

This study aimed to explore patient experience from participation in a randomised trial (INFLUENCE trial) evaluating fluorescent navigation with indocyanine green (ICG) for sentinel node localization in early breast cancer[2].

INFLUENCE is a prospective randomised study that compared ICG fluorescence combined with a standard tracer (blue dye or radioisotope) versus ICG alone for sentinel lymph node (SLN) detection in early breast cancer. The primary objective of this study was to determine the sensitivity of ICG alone for SLN identification compared with a combination of ICG and a standard tracer. Two cohorts of patients were recruited from separate centres each containing patients scheduled to undergo routine SLN biopsy. Patients within cohort 1 (Cambridge) were assigned to one of two groups and received injection of either ICG alone (n= 25) or combined with radioisotope (n= 25) for SLN localisation. Patients in cohort 2 (Dundee) were localised with either ICG alone (n=25) or combined with blue dye (n= 25). The study recruited 100 patients in total between 6 and 12 months from these two centres. Three patients were excluded with the final analysis performed on 97 patients.

Aim

To explore patient experiences and attitudes toward participation in a randomized surgical trial (INFLUENCE) evaluating indocyanine green fluorescent navigation versus standard care for sentinel node localization in early breast cancer, with particular focus on perceptions of randomization, information provision, and experimental treatment allocation.

Recruitment

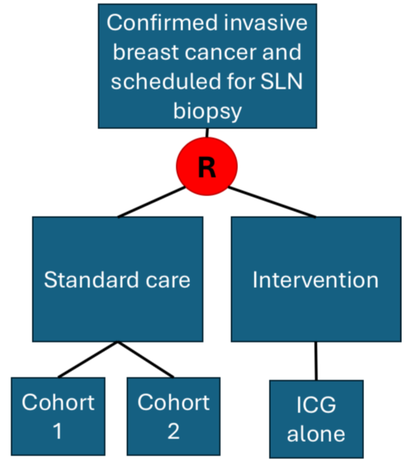


Figure 1: *Randomization Schema for Sentinel Lymph Node Biopsy in Breast Cancer*

Methods

A questionnaire was issued retrospectively to all trial patients (n=100) who took part in the INFLUENCE trial. An online google form and questionnaires were posted to patients. Key themes explored included:

- Motivation for trial *participation*
- Attitudes towards *randomization*
- Whether *information* provision was adequate
- Patient *concerns* about standard tracer agents.

The questionnaire response rate was just under half (45%). Data was quantified using a 10-point Likert scale (strongly agree [1], strongly disagree [10]). Statistical analysis employed a one-sample T-test to determine significance of deviation from the hypothesized neutral value of six. A mixed-methods approach provided holistic assessment of patients' experience with open-ended questions generating qualitative data for context. Employing a comprehensive post-study analysis, several positive messages were identified from this INFLUENCE trial that might be applied more generically to inform the design and conduct of future surgical trials.

Trial Processes

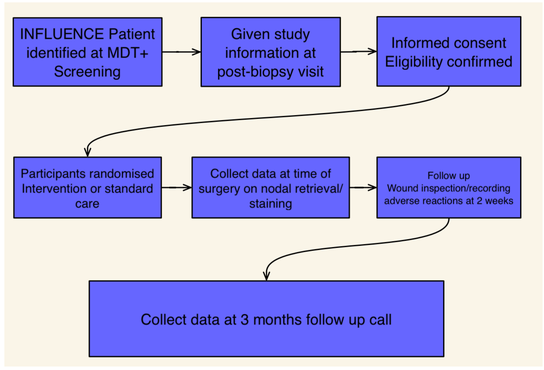


Figure 2: *Patient Pathway and Data Collection Timeline in the INFLUENCE Trial*

Results

a) *Motivation for trial participation* - a principle motivation for trial participation was a desire to help future patients (1.22; p<0.001).

b) *Random allocation* - patients appeared comfortable with randomization to different treatment groups and acknowledged the uncertainty of whether they would be allocated to the experimental or standard treatment arm. Patients understood they could not choose a particular treatment option and were obliged to accept their treatment allocation and not withdraw from the trial post-randomization (2.32; p<0.001).

c) *Experimental arm* - patients were unconcerned about any potential negative impact from being part of the experimental arm were aware that the experimental arm might be less accurate (7.5; p<0.01).

d) *Pre-trial information* – this was deemed accessible and comprehensive (1.93; p<0.001) and patients had sufficient time to process this before making any final decision on trial participation. Patients did not feel under any pressure to participate in the trial and were provided with sufficient time to think about taking part (including the opportunity to discuss with family members and friends) (1.75; p<0.001).

e) *Radioactive tracer usage* - patients were unconcerned about radioactive tracer usage and exposure to radioactivity (8.05; p<-.001).

f) *Advantages of ICG over radioisotope* - avoiding exposure to a source of radioactivity was considered an advantage of ICG alone for detection of sentinel nodes (3.67; p<0.001). It was considered an advantage not to attend nuclear medicine for a radioisotope injection on the day of surgery.

Conclusion

Results of this questionnaire are reassuring in a broader context and confirm that any barriers to trial participation are not primarily related to concerns about the randomization process or allocation to an experimental treatment arm. Furthermore, this data suggests that any pre-existing concerns can be mitigated through effective pre-trial engagement and communication with the research team. A strong sense of altruism prevails amongst patients and highlights the importance of emphasizing the benefits of clinical research to prospective trial participants. Optimal and well-written pre-trial information is essential and patients should be allowed adequate time to process this information and reflect upon trial participation. Well-designed consent processes will positively influence enrolment along with transparent dialogue and trust in the healthcare professionals conducting the study.

References

1. McCulloch P, Taylor I, Sasako M, Lovett B, Griffin D. Randomised trials in surgery: problems and possible solutions. BMJ. (2002)
2. Ingram, J., Beasant, L., Benson, J. et al. The challenge of equipoise: qualitative interviews exploring the views of health professionals and women with multiple ipsilateral breast cancer on recruitment to a surgical randomised controlled feasibility trial. Pilot Feasibility Study 8, 46 (2022)