



Using tablet-based technology in patient education about systemic therapy options for early-stage breast cancer: a pilot study

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ABSTRACT

Background Patient education in early-stage breast cancer has been shown to improve patient well-being and quality of life, but it poses a challenge given the increasingly complex regimens and time constraints in clinical practice. Technology-aided teaching in the clinic could help to improve the understanding of adjuvant systemic therapy for patients. In this prospective pilot study, we used a clinician-administered, tablet-based teaching aid to teach patients with early-stage breast cancer about adjuvant systemic therapy.

Methods Participation was offered to newly diagnosed patients with early-stage breast cancer presenting for their first medical oncology visit at a provincial cancer centre. Participants were shown a tablet-based presentation describing procedures, rationales, risks, and benefits of adjuvant systemic therapy as an adjunct to a discussion with the medical oncologist. After the clinic visit, participants completed a questionnaire measuring satisfaction with the visit and knowledge of the treatment plan discussed.

Results The 25 patients recruited for the study had a mean age of 57 years. An offer of upfront chemotherapy alone was made to 12 participants (48%), chemotherapy with trastuzumab to 4 (16%), and hormonal therapy to 9 (36%). Correct answers to all questions related to treatment knowledge were given by 22 patients (88%). Satisfaction with the clinic visit was high (mean satisfaction score: 4.53 ± 0.1 of a possible 5).

Conclusions We found that a tablet-based presentation about adjuvant systemic therapy was satisfactory to patients with early-stage breast cancer and that knowledge retention after the clinic visit was high. Tablet-based teaching could be a feasible and effective way of educating patients in the breast oncology clinic and warrants further investigation in randomized studies.

Key Words Breast cancer, patient education, mobile technology, tablet computers, adjuvant systemic therapy, e-learning, clinical teaching tools

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INTRODUCTION

In an era of expanding treatment options for early-stage breast cancer and increasingly complex therapeutic regimens, a growing body of research has focused on helping patients make informed decisions about their care. Many of those investigations have used various forms of computer-assisted learning to provide information to patients and to guide treatment decisions. By using multiple modalities (any combination of text, images, audio, and video) to transfer knowledge, computer-assisted patient education can increase the understanding and retention of treatment information by patients. Computer-assisted patient education

can also help to standardize and reinforce the information provided during a typical clinical consultation.

The use of visually-based decision aids, both computerized and non-computerized, is perhaps most firmly established in the field of surgical oncology. Interventions such as decision boards or interactive decision aids have been used to educate and guide patients with newly diagnosed breast cancer in choosing between mastectomy and breast-conserving surgery. In that patient population, such tools, as an adjunct to discussion with a surgical oncologist, lead to higher knowledge retention, decreased decisional conflict, and increased satisfaction with decision-making^{1,2}. In a study of women considering breast reconstructive

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surgery, patients retained more information and were more involved with clinical decision-making when shown a computer-learning module than when given a standard surgical consultation³. Similar interventions have been undertaken in the fields of genetic screening for breast cancer⁴ and adjuvant chemotherapy for patients with node-negative breast cancer⁵, with patients showing better knowledge retention after completing computer-based education modules.

Most of the computer-based education interventions reported to date have consisted of CD-ROM or Web-based modules that the patient completes either at home or in the clinic before or after the clinical consultation^{6,7}. Such programs can be completed either by the patient alone or with assistance from a health care provider. One potential disadvantage of such an approach is that patients might miss the chance to benefit from emotional support provided by the clinician⁴ and from the opportunity to ask questions as they arise. One way to address those issues would be to integrate computer-based teaching into the clinical encounter, as a tool to be used during discussion of treatment options.

Within the realm of breast oncology, we found one such intervention, in which a computer-based education tool was used to teach breast cancer patients about surgery, radiation, and systemic therapy^{8,9}. Pruthi *et al.* found that patients were equally satisfied with both computer-based and traditional teaching, and the computer-based teaching did not increase the length of the clinical visit. In a follow-up letter, the authors noted that patients receiving the computer-based teaching significantly improved their knowledge of treatment information⁹. However, the authors did not describe the type of computer (for example, tablet vs. desktop) used in the intervention or how the computer was incorporated into the clinical encounter. Those aspects are potentially important, because computer use in the clinic could act as a barrier and have a detrimental effect on patient satisfaction^{10,11}.

The recent widespread availability of tablet computers could represent an opportunity to bring computer-based teaching into the clinic without compromising patient-physician interaction, because these devices can easily be held and displayed without disrupting eye contact or patient-physician interaction. Thus, the goal of our study was to pilot a tablet-computer-based teaching tool for use during discussion of adjuvant systemic therapy in patients with newly diagnosed breast cancer. The use of a tablet-computer-based education tool could provide the patient with individualized information in multiple modalities (images, text, and speech), tailored to their diagnosis and therapeutic plan, during their discussion with a medical oncologist. In the present study, we assessed patient satisfaction and knowledge retention after their first medical oncology visit, which featured a discussion of adjuvant systemic therapy incorporating a tablet-computer-based education tool.

METHODS

Patient Population

The Dr. H. Bliss Murphy Cancer Centre is located in St. John's, Newfoundland and Labrador, and serves as the

primary site for evaluation and treatment of patients with cancer in the province. The catchment area includes both the island and the mainland portion of Labrador, with a population of 514,536¹². The province has the most linguistically homogenous population in Canada, with 95.7% of residents reporting English as their only language¹³.

Patients with a new diagnosis of stage I-III breast carcinoma who were referred to Medical Oncology at the Dr. H. Bliss Murphy Cancer Centre for consideration of adjuvant systemic therapy were offered enrolment in the study at their first medical oncology visit. Patients were excluded if they were deemed not suitable for systemic therapy by the treating medical oncologist, if they were unable to read and understand spoken English, if they had significant visual or hearing impairment, if they had a psychiatric or cognitive disorder that would preclude them from participating in a discussion of therapy, or if they were unwilling to give informed consent to participate in the study. Approval was obtained from the provincial ethics board before commencement of the study. All patients provided written informed consent before participating.

Intervention

The intervention consisted of a multimedia slideshow, including text, images, and diagrams illustrating the rationale for adjuvant systemic therapy; the benefits, risks, and potential adverse effects of treatment; and the treatment schedule. The content of each presentation was chosen based on the therapy that the patient would be initiating first—that is, a patient offered chemotherapy followed by hormonal therapy would be shown a presentation about the chemotherapy portion.

The participating medical oncologist used an iPad (Apple, Cupertino, CA, U.S.A.) handheld tablet computer to show the slideshow to the patient. The intervention was used as an adjunct to discussion with the medical oncologist, and the patient was encouraged to ask questions during the presentation. Content was tailored to the specific treatment regimen offered.

The presentations were created by ERM using Prezi (<http://prezi.com>), a nonlinear presentation platform that allows users to zoom in so as to focus on important content. All content was evaluated and approved by the participating medical oncologists. A fully functional sample presentation can be viewed at http://prezi.com/gv-tf15hi5ax/?utm_campaign=share&utm_medium=copy&rc=ex0share.

The content of the presentations was reviewed by all breast medical oncologists practicing in the province. The presentations were used as a visual aid during discussion of adjuvant treatment. The tablet was operated by the physician and shown to the patient to illustrate the spoken points and to guide discussion of the proposed therapy. Although the presentations proceeded in a set structure (rationale for treatment, overview of the treatment regimen, side effects, and when to seek medical advice), the oncologist could stop at any point and return to previous topics or images. The physician was allowed to adapt the presentation to his or her own discussion style and could zoom in to highlight various aspects of the presentation (for example, a calendar illustrating the treatment schedule) when further

clarifying patient queries. Patients did not have access to the presentations for review either after discussion with the medical oncologist or at home. Non-study written material was available to all patients as part of usual care.

Eligible patients were given information about the study upon registering for their first clinic visit. They were given the chance to discuss the study with, and to ask questions of, the participating physician.

Outcome Measures

Two primary outcomes were measured: patient satisfaction and knowledge retention. Immediately after the clinic visit, patients completed a written questionnaire designed to evaluate their educational background and experience with technology, to test their basic understanding of the information presented, and to assess satisfaction with the intervention and the clinical encounter overall.

Knowledge retention was assessed by a 5-item questionnaire that tested understanding of the basic information conveyed during the presentation, including the goals of adjuvant systemic therapy, common side effects of treatment, and symptoms that should lead the patient to seek medical attention. The questions were presented in a multiple choice format, with 4 response options each. Questions were tailored to the type of therapy being offered. Knowledge was scored out of 5 (each correct answer scored 1 point). Table I illustrates the knowledge retention questionnaire administered to patients receiving chemotherapy without trastuzumab.

Satisfaction was evaluated using an 8-item questionnaire. Each item consisted of a statement concerning the patient's attitude toward the clinical encounter (for example, "I am comfortable with my decision to undergo or not undergo chemotherapy or hormonal therapy," "The iPad presentation helped me understand the information given by my doctor"). The items were followed by a Likert response scale of 1 (strongly disagree) to 5 (strongly agree). Overall satisfaction was scored as the mean response across all 8 items.

Statistical Analysis

Descriptive statistics for the demographic and clinical characteristics of the patients were calculated using IBM SPSS Statistics (version 22; IBM, Armonk, NY, U.S.A.).

RESULTS

Between 1 February and 30 April 2012, 25 patients were screened and consented to participate. All patients who initially consented to participate in the study went on to complete the intervention and the post-encounter questionnaires. Table II shows the demographic and clinical characteristics of the patients. Mean age was 57 years (range: 38–69 years). Of the 25 patients, 12 (48%) were offered chemotherapy, 4 (16%) were offered chemotherapy with trastuzumab, and 9 (36%) were offered hormonal therapy. One patient with HER2-positive disease declined adjuvant chemotherapy with trastuzumab and was offered upfront hormonal therapy.

Table III shows the experience and comfort the patients expressed about the technology. As shown, 14 patients

TABLE I Sample knowledge retention questionnaire (chemotherapy without trastuzumab)

1.	My treatment consists of ____ cycles of chemotherapy.
	a) 4
	b) 6
	c) 8
2.	Adjuvant chemotherapy is:
	a) Given to guarantee that the cancer will not come back.
	b) Given to destroy cancer cells left after surgery.
	c) An alternative to surgery for breast cancer.
	d) Given to decrease nausea and vomiting.
3.	If you develop a high fever while on chemotherapy, you should:
	a) Make an appointment to see your doctor in 2–3 days.
	b) Take Tylenol and drink lots of fluids.
	c) See your doctor immediately or go to the Emergency Department.
	d) Do nothing—this is a normal response to chemotherapy.
4.	Each cycle of chemotherapy will last:
	a) 1 week
	b) 2 weeks
	c) 3 weeks
	d) 4 weeks
5.	Common side effects of chemotherapy include:
	a) Acne
	b) Nausea, vomiting, and hair loss
	c) Hallucinations
	d) Hiccups

(56%) reported that they frequently used computer technology at home, and most patients described themselves as "fairly comfortable" (52%) or "very comfortable" (12%) using computer technology.

As Table IV illustrates, satisfaction with the consultation and the clinic visit was high, with a mean satisfaction score of 4.53 ± 0.1 of a maximum score of 5. Although the sample size was small, satisfaction did not appear to vary with age, disease stage, treatment modality offered, education level, or self-reported comfort with technology. Knowledge retention was high, with 22 patients (88%) answering all 5 questions correctly, and all participants correctly answering at least 3 of 5 questions.

DISCUSSION

In this prospective pilot study of a tablet-based tool for teaching early-stage breast cancer patients about adjuvant systemic therapy, we found that patients were satisfied with the intervention and that knowledge retention about the goals, risks, and benefits of treatment was high after the clinic visit. The effect seemed consistent regardless of self-reported comfort with technology, education level, or clinical diagnosis.

TABLE II Demographic and clinical characteristics of the women in the study group

Characteristic	Value
Patients (n)	25
Age (years)	
Mean	57
Range	39–69
Regional health authority [n (%)]	
Eastern	18 (72)
Central	3 (12)
Western	3 (12)
Labrador–Grenfell	1 (4)
Stage [n (%)]	
IA–C	8 (32)
IIA–C	13 (52)
IIIA–C	4 (16)
Receptor status [n (%)]	
ER or PR-positive, HER2-negative	18 (72)
ER or PR-positive, HER2-positive	5 (20)
Triple-negative	2 (8)
Treatment offered [n (%)]	
Chemotherapy	12 (48)
Chemotherapy + trastuzumab	4 (16)
Hormonal therapy	9 (36)
Highest level of education [n (%)]	
≤Grade 6	0
Grade 7–9	1 (4)
Grade 10–12	8 (32)
Community college or trade school	12 (48)
University	4 (16)

ER = estrogen receptor; PR = progesterone receptor; HER2 = human epidermal growth factor receptor 2.

Our findings are supported by a growing body of evidence that computer-based interventions can be helpful in a variety of clinical contexts, including oncology^{7,14,15}. To our knowledge, no previous studies have used tablet-based education in the context of adjuvant breast cancer therapy. A similar intervention was used to educate lung transplant recipients about adherence to immunosuppressive therapy¹⁶. The primary outcome in that study was treatment adherence (measured by serum drug levels), and the tablet-based education tool was found to be noninferior to conventional nurse-administered teaching, with a trend toward better adherence in patients receiving the tablet-based intervention.

Use of computer-based clinical teaching in oncology and other medical settings continues to increase, and there

TABLE III Patient-reported comfort with technology

Variable	Value [n (%)]
Computer use at home	
Never	4 (16)
Rarely	2 (8)
Sometimes	5 (20)
Frequently	14 (56)
Computer use at work	
Never	9 (36)
Rarely	0
Sometimes	1 (4)
Frequently	7 (28)
Not available	8 (32)
Comfort with technology	
Very uncomfortable	3 (12)
Somewhat uncomfortable	3 (12)
Fairly comfortable	13 (52)
Very comfortable	6 (24)

is evidence that it is a useful and cost-effective way to educate patients^{6,7}. However, the widespread use of electronic medical records has also made it clear that computer use during the clinical encounter can also act as a barrier, particularly when it results in loss of eye contact between patient and physician^{10,11}. Computer-based teaching using a standard desktop computer might be less than optimal, because the positioning needed for the patient to have an unobstructed view of both the computer screen and the clinician is difficult to achieve in a typical examination room. Use of a tablet computer could allow doctors to integrate computer-generated educational material and visual aids into discussions about treatment options while maintaining the benefits of face-to-face interaction.

Patients were very satisfied with their clinic visit and with the tablet-based intervention, and satisfaction did not differ according to stage of disease, treatment offered, or prior experience with technology. Previous studies in oncology patients of satisfaction with patient–physician interaction have shown high levels of reported satisfaction that do not vary with sex, tumour type, or intent of treatment (cure, remission, palliation, etc.)¹⁷. Younger age has been associated with lesser satisfaction, with the lowest satisfaction being seen in patients under 25 years of age and the highest satisfaction in patients more than 60 years of age¹⁷.

Our results are encouraging—in particular, the high degree of knowledge retention found immediately after the clinic visit. All 25 patients were able to identify that the intent of adjuvant systemic therapy is to reduce the risk of cancer recurrence, but that it could not completely eliminate the possibility of relapse. That observation is significant given the relative complexity of discussions

TABLE IV Patient satisfaction scale and mean scores (*n* = 25)

Survey Item	Score	
	Mean	Range
1. I am comfortable with my overall clinic visit experience.	4.5±1.1	1–5
2. I have a good understanding of the treatment options discussed today.	4.5±1.0	1–5
3. I am comfortable with my decision to undergo or not undergo chemotherapy or hormonal therapy.	4.6±0.9	1–5
4. Information about chemotherapy was presented in way that I was able to understand.	4.7±0.9	1–5
5. The iPad ^a presentation was a useful tool during today's appointment.	4.6±1.0	1–5
6. The iPad ^a presentation helped me understand the information given by my doctor.	4.6±0.9	1–5
7. The iPad ^a presentation helped me remember the information presented.	4.4±1.2	1–5
8. I would like to see technology such as iPad ^a used in future presentations by a nurse or physician.	4.5±1.0	1–5

^a Apple, Cupertino, CA, U.S.A.

about adjuvant systemic therapy and the fact that patients with early breast cancer have been shown to overestimate the benefit of adjuvant therapy and to have a poor understanding of treatment goals¹⁸. For example, in one study of the effects of physician communication style on patient understanding of treatment goals, only 43%–55% of patients could correctly identify the goal of adjuvant therapy for breast cancer¹⁹. Good communication of treatment information has been linked to better adherence to treatment, an increased sense of control, and decreased psychological distress in patients with a new diagnosis of cancer^{17,20}.

Limitations

As a small nonrandomized project, this study did not allow for comparison with a control group of patients receiving standard physician- or nurse-administered teaching. Thus, although the degree of knowledge retention was encouraging, we cannot be certain that the tablet had an independent effect on the understanding of treatment information expressed by the patients. The fact that almost all patients answered all questions correctly might indicate that our measurement tool has underestimated the degree of knowledge retention immediately after a discussion of adjuvant therapy. A short 5-item questionnaire was chosen to help minimize the extra time required for patients to participate in our study; a longer, more detailed evaluation might increase sensitivity to variation in patient understanding, but might also jeopardize the willingness of some individuals to participate or to complete the evaluation.

Clinician satisfaction with the tool and its effect on clinic workflow was not formally assessed, limiting our ability to determine whether this approach is likely to be useful as an everyday clinical tool.

Patients were quite satisfied with the intervention and with the clinic visit overall, but the validity of reported satisfaction as an outcome measure in oncology has been questioned because patients place tremendous faith in the treating clinician and could be reluctant to criticize practice in case it jeopardizes their treatment or care¹⁷. Thus, judging patient satisfaction with an intervention in oncology might require more careful investigation to accurately capture any effect on patient well-being.

Future Directions

The widespread availability and increasing affordability of tablet computers make them an ideal tool for education in the clinical setting. Although our intervention was administered by the treating oncologist during a discussion of treatment options, the same format could also be used as a nurse- or pharmacist-administered tool. In addition, many technology-based patient education studies in the field of breast oncology have used patient-administered tools either during the clinic visit or at home over an Internet connection with encouraging results⁷. Our presentations could easily be made available for the patient to access at home as a Web page or mobile telephone app to review treatment information; they could also incorporate links to further information about side effects and management, sources of support, and contact information in case of further questions or concerns. Such a platform could also be expanded to provide appointment and medication reminders and to allow patients to record and report side effects and toxicity, with results made available to the treatment team. Concerns about side effects could direct the patient to suggestions for self-management (where appropriate) and provide guidance about when medical assistance is indicated. The continued evolution of mobile technology will likely lead to further possibilities and applications.

The next step in the evaluation of our tool will be a randomized trial comparing use of the tablet computer-based presentations with usual care. We hope to compare satisfaction and knowledge retention between treatment groups, to further explore the effects on those outcomes throughout the course of therapy, and to evaluate acceptability and efficiency for clinicians of the tablet-based intervention.

CONCLUSIONS

Although the results reported here require confirmation in a randomized controlled setting, our findings suggest that a tablet-based teaching tool is feasible and satisfactory to patients with early-stage breast cancer embarking on adjuvant systemic therapy. Knowledge retention immediately after the clinic visit was high, suggesting good comprehension of the information provided. Overall, our findings support emerging

evidence that tablet-based teaching is a potentially useful tool for patient education in oncology and other areas of medicine.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare the following interests: KL has received fees as an advisory board member for Amgen, Celgene, and Roche. JM has received fees as an advisory board member for Bayer, Novartis, Roche, and Janssen. MDS has received research funding and honoraria from Roche.

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REFERENCES

- Whelan T, Levine M, Willan A, *et al.* Effect of a decision aid on knowledge and treatment decision making for breast cancer surgery: a randomized trial. *JAMA* 2004;292:435–41.
- Waljee JF, Rogers MA, Alderman AK. Decision aids and breast cancer: do they influence choice for surgery and knowledge of treatment options? *J Clin Oncol* 2007;25:1067–73.
- Lee BT, Chen C, Yueh JH, Nguyen MD, Lin SJ, Tobias AM. Computer-based learning module increases shared decision making in breast reconstruction. *Ann Surg Oncol* 2010;17:738–43.
- Green MJ, Peterson SK, Baker MW, *et al.* Effect of a computer-based decision aid on knowledge, perceptions, and intentions about genetic testing for breast cancer susceptibility: a randomized controlled trial. *JAMA* 2004;292:442–52.
- Whelan T, Sawka C, Levine M, *et al.* Helping patients make informed choices: a randomized trial of a decision aid for adjuvant chemotherapy in lymph node-negative breast cancer. *J Natl Cancer Inst* 2003;95:581–7.
- Wofford JL, Smith ED, Miller DP. The multimedia computer for office-based patient education: a systematic review. *Patient Educ Couns* 2005;59:148–57.
- Ryhänen AM, Siekkinen M, Rankinen S, Korvenranta H, Leino-Kilpi H. The effects of Internet or interactive computer-based patient education in the field of breast cancer: a systematic literature review. *Patient Educ Couns* 2010;79:5–13.
- Pruthi S, Rausch S, Montori V, Hathaway JC, Vickers Douglas KS. Patient and clinician opinion of computer-based breast cancer education during a specialist consultation. *Breast J* 2010;16:564–6.
- Collins NM, Vickers KS, Hathaway JC, Croghan IT, Pruthi S. Improving breast cancer knowledge: the use of a computerized breast cancer education tool during a clinical consultation with a breast specialist. *Breast J* 2014;20:207–9.
- Asan O, Montague E. Technology-mediated information sharing between patients and clinicians in primary care encounters. *Behav Inf Technol* 2014;33:258–69.
- Shachak A, Reis S. The impact of electronic medical records on patient–doctor communication during consultation: a narrative literature review. *J Eval Clin Pract* 2009;15:641–9.
- Statistics Canada. Table 051-0005—Estimates of population, Canada, provinces and territories, quarterly (persons) [Web resource]. Ottawa, ON: Statistics Canada; 2014. [Available at: <http://www5.statcan.gc.ca/cansim/a05?lang=eng&id=0510005>; cited 9 August 2014]
- Statistics Canada. Population by mother tongue and age groups (total), percentage distribution (2011), for Canada, provinces and territories [Web resource]. Ottawa, ON: Statistics Canada; 2011. [Available at: <http://www12.statcan.ca/census-recensement/2011/dp-pd/hltfst/lang/Pages/highlight.cfm?TabID=1&Lang=E&Asc=1&PRCode=01&OrderBy=999&View=2&tableID=401&queryID=1&Age=1>; cited 9 August 2014]
- Fox MP. A systematic review of the literature reporting on studies that examined the impact of interactive, computer-based patient education programs. *Patient Educ Couns* 2009;77:6–13.
- Mark TL, Fortner B, Johnson G. Evaluation of a tablet PC technology to screen and educate oncology patients. *Support Care Cancer* 2008;16:371–8.
- Suhling H, Rademacher J, Zinowsky I, *et al.* Conventional vs. tablet computer-based patient education following lung transplantation—a randomized controlled trial. *PLoS One* 2014;9:e90828.
- Shilling V, Jenkins V, Fallowfield L. Factors affecting patient and clinician satisfaction with the clinical consultation: can communication skills training for clinicians improve satisfaction? *Psychooncology* 2003;12:599–611.
- Hack TF, Degner LF, Parker PA on behalf of the SCRIN Communication Team. The communication goals and needs of cancer patients: a review. *Psychooncology* 2005;14:831–45.
- Siminoff LA, Ravdin P, Colabianchi N, Sturm CM. Doctor–patient communication patterns in breast cancer adjuvant therapy discussions. *Health Expect* 2000;3:26–36.
- Leighl N, Gattellari M, Butow P, Brown R, Tattersall MH. Discussing adjuvant cancer therapy. *J Clin Oncol* 2001;19:1768–78.