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Prognostic imaging in neoadjuvant chemotherapy of locally-advanced breast cancer should be cost-effective

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Abstract

Introduction—The use of neoadjuvant chemotherapy in cases of locally advanced breast cancer has been steadily increasing, and is also in wider use for other cancers. As a consequence, a growing number of studies have focused on the question of how best to assess the therapeutic response to various chemotherapy or systemic therapy regimens. Prognostic imaging of response to therapy early in the course of a planned chemotherapy regimen could be of considerable value, particularly if shifting to another therapy regimen would be more effective.

Methods—A cost effectiveness analysis was completed, specific to imaging of neoadjuvant chemotherapy response in breast cancer, to determine the dominant parameters that would make imaging systems cost effective. The cost analysis was completed with respect to a system for near infrared spectral imaging, but the costs are not dramatically different for other systems such as PET or MRI. Using a standard metric of \$25,000 per discounted life year gained as a measure of a successful system.

Results—It is shown that system specificity and patient average life expectancy are not dominant factors. Increases in cure rate and the efficacy of the initial chemotherapy are dominant factors. As long as the initial chemotherapy was less than 90% effective, most imaging systems would be cost effective, and if the cure rate of the disease could be increased as little as 1% through a change to alternate therapy, then the cost effectiveness of the system would be acceptable.

Conclusions—Based upon this simple economic analysis, diagnostic imaging of neoadjuvant chemotherapy appears warranted, assuming that it can be shown that the early shift from ineffective neoadjuvant chemotherapy to a more effective one has a measurable benefit in cure rate. This study indicates that the most important issue is to assess the added benefit of

individualized chemotherapy in patient management, and clinical trials in this area would then provide the data required to justify analysis of prognostic imaging procedures.

Keywords

Cost-effectiveness; Neoadjuvant; Chemotherapy; Prognostic; Imaging; Near-infrared; Breast cancer; Model; Cost; Spectroscopy

Introduction

Medical imaging systems are routinely used for breast cancer screening, and for cancer staging prior to treatment. A variety of diagnostic imaging modalities have a longstanding role in monitoring of therapy among those with advanced metastatic breast cancer, however the role of various conventional radiographic diagnostic imaging modalities in monitoring neoadjuvant therapy has received more limited clinical use and evaluation. While staging of breast cancer based upon size of the primary cancer and extent of axillary lymph node involvement is important in surgical planning, it is possible that significant decreases in health care cost, and significant improvements in long-term clinical outcomes, could be made if effective imaging modalities had proven utility at intermediate points during the course of neoadjuvant chemotherapy (NACT) [1].

NACT is widely used in locally advanced breast cancer (LABC) and has good potential use in many other types of locally advanced cancer. Neoadjuvant chemotherapy has been shown in numerous studies to be effective in “down staging” many patients with LABC, allowing the use of breast conservation, or lumpectomy and radiation therapy [2], rather than a more extensive mastectomy. Current clinical practice does not routinely use imaging to determine which women are responding to the NACT until after completion of their treatment, so there is little definitive evidence about the ability to switch patients to different treatments mid-course. Thus, the question of whether to complete the planned course of NACT or terminate this first-planned regimen early, and in place begin other conventional therapy is difficult to evaluate. Alternatively, newer investigational therapies could be used in those with a very poor prognosis, and therefore beginning a therapy which might have more promise, is a critical and timely issue in individualizing patient management. The extent to which imaging can have a substantive role in this decision making process, and the logistical benefit of ending the course of therapy early are questions that need to be addressed. This paper examines the economic aspect of this by evaluating the cost-effectiveness of using the results from an imaging modality to intervene early in the course of NACT for LABC, based upon a pre-defined measurement of “response” which is deemed to be prognostic.

There is growing evidence that the primary cancer response can be accurately imaged either with contrast-enhanced MRI [3], positron emission tomography (PET) scanning, or newer imaging systems such as near-infrared hemoglobin imaging, although there is much less conclusive evidence on the accuracy of this latter modality imaging. A complicated part of this strategy is the fact that there are known inaccuracies in predicting the change in size of cancer, either primary or metastatic [4–7], and the fact that errors in sizing appear to be unexpectedly large. Interestingly, several studies have recently shown that imaging markers with MRI [4,7] or nuclear medicine overestimate the response to therapy [8], as measured by the tumor size. Unfortunately, even assessing cancer response in pathology is not uniformly defined. Thus, since the pathologic assessment of response has become the “gold standard” to which imaging would be compared [9], it makes assessing these modalities subject to a higher level of uncertainty. Despite these uncertainties, there is evidence that contrast-enhanced MRI could actually be superior to standard clinical assessment methods in determining the prognostic response to NACT [10,11]. One important conclusion about

imaging breast cancer during NACT is that at least some studies based on anatomic imaging, such as ultrasound, have shown poor ability for prognostic response [12], indicating that more functional assessment may be of much greater utility. Studies with nuclear medicine methods appear promising [13], yet there are reports, suggesting that the uptake of Tc99-Sestimibi over-predicts this response to therapy [13]. Thus, it is possible that cellular metabolism is not the best marker to measure in LABC with potentially multi-centric or multi-focal components.

Recent pilot studies in both MRI and Near-Infrared Spectroscopy (NIR) have shown that more global estimates of cancer, such as water content and vascular volume changes, can be good predictors of response in primary breast cancer [14–18]. Total water content and vascular volume are robust signals in that they can be measured with a good signal to noise ratio, and biological variations in these are generally low, except in response to intervention. Further, and of great potential interest, in pilot studies there is evidence that these biophysical changes occur within the first cycle of chemotherapy [14–18], which could have considerable prognostic value if confirmed with high specificity. Thus a key factor being tested in multi-center trials now is to determine the sensitivity and specificity of NIR or MRI as a measurement of response within the first cycle of NACT, and if this value is sufficient for a cost-effective test. It is also likely that the imaging alone would not be sufficient, but that imaging combined with clinical examination or other low-cost markers could be used. This study examines what range of performance characteristics are required for imaging to provide a cost-effective means of tailoring NACT early in the treatment cycle.

Methods

Clinical strategies analyzed

A key factor in modeling cost-utility is to determine the flow chart for patient management, placing numbers on “typical” pathways. The conceptual models of how patients would be managed are shown in Fig. 1, with the standard of care today, shown in (a), and then an initial attempt at introducing imaging in (b) assuming a perfect imaging system. Finally, this is followed by the complete model with an imperfect imaging system in (c). The latter model shown in (c) was used throughout the numerical modeling shown here, and the first two models are simply shown to illustrate the conceptual design process.

Standard care model for neoadjuvant chemotherapy

The standard care model is the flow chart in Fig. 1a, using the key point of response or no response following the complete initial regimen of NACT. This model has no intervention in the pathway. Instead, there is simply one full sequence of NACT followed by surgery, or if there is no response, the possibly a second approach to therapy prior to surgery. The specific NACT regimens will vary somewhat among different oncologists, but essentially the goal is to downstage the cancer in the first 6 months with NACT. This will increase the likelihood of less invasive surgery (lumpectomy vs. mastectomy). Roughly 70% of patients will have pathology confirmed complete or partial response (CR + PR) to treatment and the other 30% will not have at least a partial response [19]. Later these numbers are varied to study their influence. Those who do respond will go on to have definitive treatment (surgery ± radiation) and the overall prognosis can be quite good, but varies depending on the initial stage and pathologic subtype of the tumor. Those who do not respond will potentially receive alternative chemotherapy (NACT II), or newer investigational therapy and most will ultimately advance to surgical mastectomy, with or without radiation therapy to the chest wall. These patients face a less favorable outcome (perhaps 20–50% cure rate) and undergo more costly and aggressive treatment. Additionally, several months were spent waiting for

an NACT regimen to work, which ultimately did not. The clearly unanswered question is: do those 6 months of ineffective therapy negatively impact the resulting survival?

The number of women undergoing neoadjuvant therapy is not critical for this analysis, as the model was evaluated based upon dollars per life year gained. So it was a normalized societal population that entered the flow chart model, for the calculations on the US population. Having this “base case”, allows introduction of the new technology, to see how the flow chart and related outcomes would change.

Basic imaging intervention model for neoadjuvant chemotherapy

The pilot data in NIR and MRI indicate that they might predict whether there is a potential ‘imaging response’ to NACT within the first cycle of NACT, and the eventual goal would be to assess the prognostic accuracy of these systems for the correlation with pathologically defined complete response (CR), partial response (PR) or no response (NR). Several such pilot trials are ongoing now. If there was a measurable CR or PR demonstrated early in treatment, then the patient would follow the normal course to complete their planned treatment. However if no imaging response was expected, based upon prognostic imaging, then an altered treatment regimen would be given 4–6 months earlier. This flow chart is shown in Fig. 1b. Although breast cancer is not one of the fastest growing, nor most aggressive cancers, 6 months may be a sufficient time for some women's disease to progress to a more advanced status, which is harder to cure. Clearly, if nothing else, this approach would spare a patient from ongoing therapy with a certain incidence of toxicity, and a small but real risk of serious toxicity, that will have no therapeutic benefit. However the strategy studied here relies upon the concept that earlier therapy would have a measurable impact on life expectancy. This is an untested hypothesis which will be revisited in the “Discussion” section.

Complete imaging intervention model for neoadjuvant chemotherapy

The final version of the computational flow model, shown schematically in Fig. 1c, acknowledges an imperfect imaging systems by incorporating the sensitivity and specificity of the procedure. These performance characteristics are often the main factor in determining the effectiveness of a new technology, and may be assessed through multicenter trials. While performance characteristics are not known with certainty, increasing numbers of false positives and negatives obviously would impact the cost effectiveness, and must be modeled. Here the false positives are treated as though they were positively responding to therapy, even though they were not, and their net shorter lifespan would adversely affect the cost per life year gained. False negatives cases are more difficult to understand in that the imaging test indicates they are not responding when they actually were, and were inadvertently switched to a new NACT. This could result in overall harm relative to a strategy with no intervention early in the course of therapy. As described below, it was assumed that the unnecessary treatment switch prompted by a false negative would result in no measurable change in survival.

The model in Fig. 1c was used throughout this study to evaluate: (1) the medical benefit for having this technology measured in terms of life years gained (LYG) and (2) the cost of providing this technology. Model assumptions and base-case parameters are described in the next section.

Model assumptions and base case parameters

Table 1 shows initial input parameter values for sensitivity, specificity, and responder prevalence, which were all initially set at 70%, along with estimates of true negative, false

negative, true positive and false positive outcomes. Additional estimates that went into these calculations are summarized below.

Cure rate—Approximately 59% of women initially failing NACT (and later receiving a different therapy + surgery ± radiation) will be “cured” from their disease, which we refer to as the cure rate. The introduction of imaging is hypothesized to increase this number above 59%, and is likely to be only a few percent in cure rate does not refer to the cure rate for the whole population, only for those who would eventually fail initial NACT because this is the only group for which the imaging technology may help.

Life expectancy—The incidence of disease by age bracket was retrieved from the American Cancer Society and converted into incidence within each decade, and is reported in Table 2. These values were converted from “with respect to all women” to “with respect to all women who eventually present with LAD”. By assuming that women who present in their 40s are, on average, 45 years old, and that if they fail treatment, they will die within 5 years to determine their age at death. Then, based on 2002 US life tables [20] the normal life expectancy of women at the same age was computed using a 3% per year discount rate. The difference between discounted remaining life expectancy for disease free women and 5 year survival for those failing treatment was used as a conservative estimate discounted life years gained. The average LYG was estimated as a single value by taking the population distribution to weight the numbers in the LYG column (Table 2), and a population-weighted average LYG was estimated.

Cost-effectiveness analysis

To address the economic value of prognostic imaging, calculations were based on a population size of 213,000 new diagnoses of LABC each year. Estimated device costs for this population were based on similar systems and expected hospital costs as detailed below. Imaging system costs for the population were weighed relative to the projected gains in life years for a population undergoing imaging in comparison to standard care. Cost-effectiveness for prognostic imaging is expressed as cost per life year gained.

Device cost—The imaging device itself was assumed to have an initial cost of \$1,000,000, and to have a 10-year useful lifespan. At a hospital's Cost of Capital of 9%, each imaging device would have a capital cost of \$155,820 per year. Associated technician cost was assumed to be \$200,000 per year, making a total annual cost of \$355,820 per machine. For a population of 213,000 women diagnosed with LABC per year, it is assumed that there would be an average of 1.3 exams per year for a total of 276,900 exams per year. Assuming each device scans 10 people per day 5 days per week over 50 weeks per year would require 111 machines for the US population (computed as $[213,000 \times 1.3] / [50 \times 10 \times 5]$). Thus, the national cost of implementing prognostic imaging is estimated at \$39,496,030. To address economic value, this total cost was weighed relative to the projected gains in life years for the population of 213,000 women.

Ratio of cost per life year gained—To compute the cost per life year gained for prognostic imaging relative to standard care, the increase in the number of lives saved is estimated based on the difference in the cure rate with prognostic imaging relative to standard care. The number of lives saved are then multiplied by the discounted life expectancy (Table 2) to estimate total life years gained for the population. Total imaging costs are then divided by total life years gained to estimate the cost-effectiveness of prognostic imaging. For example, under standard care the cure rate is modeled as 59%. Increasing this by 2–61% with prognostic imaging increases the number of lives saved relative to standard care by 895 lives and 8,055 life years (895×9). Thus, cost per life year

gained is \$4,903 ($\$39,496,030/8055$) when the cure rate is increased by 2% with prognostic imaging.

Initial estimate of cost per exam: hospital perspective calculations

Much of the driving force for new technologies comes at the local hospital level, and so it is important to assess the cost-effectiveness of the individual device and procedure from the medical center perspective. Using the same data, plus additional institution-specific cost estimates, the cost per exam can be estimated. The values were estimated for one medical center were used to arrive at a break-even price that the hospital would have to charge to cover all device-related expenses. Cost per life year gained were also computed for a single institution.

Sensitivity analyses

Quantifying the economic potential of prognostic imaging depends on several factors, some that are evidence-based and some that are assumptions about the technology itself. Some input parameters were so uncertain that their values were systematically varied over the entire possible range, in order to understand how their values would impact the estimated \$/LYG. The first such parameter was the cure rate. If this number is just larger than 59%, say 59.5%, then there is little benefit for these women and it should be expected that a high \$/LYG would result. However, if this cure rate is large, then it is more cost effective. The second key parameter to be examined was the *prevalence* of individuals who will respond to NACT. As the prevalence increases, then fewer women will be helped by the technology, and the \$/LYG would be expected to increase. The specificity and sensitivity of the imaging are key unknown parameters, so sensitivity analysis was completed on these parameters. Finally, changes in the assumed life-expectancy among those completely failing treatment was also examined.

Results

As shown in Table 3, for a population of 213,000 diagnosed with LABC, following the flow charts of Fig. 1 with input parameters as specified in Table 1, the total number of persons cured is 171,891 with standard care and 172,786 with prognostic imaging. The total number deceased within 5 years is 41,109 under standard care and 40,214 with prognostic imaging. Thus, 895 fewer women die within 5 years with projected expectancy gains totaling 8,055 years. This results in a cost per life year gained of \$4,903 for prognostic imaging relative to standard care.

Cost per exam from hospital perspective

Figure 2 displays cost per exam as a function of the number of new cases of women slated to receive NACT each year. In the cost effectiveness calculations, shown in (b), the values for the institution are shown as a function of the number of cases at one hospital. The discontinuities in this curve result from the fact that a medical center must purchase an integer number of machines, and so jumps in the \$/LYG occur at each point where an additional device would have to be obtained to service the patient load. Interestingly, the annual patient volume ideally probably needs to be in the range of greater than 300 cases per year to ensure that the cost per life year gained is reasonable, and the cost per exam is reasonable.

Sensitivity analyses

The sensitivity of each of the four most influential parameters was analyzed for effect upon on the estimated cost/LYG. These were (a) prevalence of responders from the initial or

primary NACT, (b) the life expectancy for those failing initial treatment, (c) the specificity of the imaging system, and (d) the increase to the cure rate from the secondary NACT regime. These are all shown in Fig. 3 in the panels a–d, respectively.

Figure 3a demonstrates the non-linear dependence of \$/LYG on the prevalence of responders as measured by imaging, meaning the fraction of women would not have their treatment altered by the imaging procedure. At 70% prevalence, the device shows good promise for being cost-effective, but as the imaging responder prevalence increases to the primary NACT (and less women benefit from the assessment) the cost effectiveness changes markedly. In assessing any imaging system, it will be crucial to accurately assess what percent of women would not have their treatment altered by the use of the technology because even if it is a perfectly accurate device, its value lies in its ability to change treatment plans, not just to predict future outcomes. The current rate of pathologically defined responders and 5 year survival for NACT patients is believed to be 59%, and it seems unlikely that dramatic increases in this number will be seen for sometime, this parameter is likely not a major factor in determining the cost effectiveness.

Figure 3b shows the minimal impact that mean survival among those completely failing treatment has on the \$/LYG. Since mean survival estimate is taken to be 5 years, this parameter is not going to have a major impact upon estimating cost effectiveness of imaging.

Figure 3c shows how the cost effectiveness increases with the specificity of the imaging system. Although it is difficult to know the specificity of the imaging system until a clinical trial is completed, 70–80% is the most likely minimum value for systems in use today. Even if the specificity was quite low, the cost effectiveness would be within an acceptable range, indicating a fairly weak dependence upon this parameter. Thus, calculations with a 70% value can be reasonably extrapolated on a linear scale.

Figure 3d shows that even modest improvements in the 5 year cure rate, which is 59% with current treatment practices, resulted in marked decreases in \$/LYG. For clarity, the graph in (d) is shown as the increase in the cure rate, such that 0% corresponds to the expected 59% which is achieved already with the primary NACT. Even an increase to 1% or 2% survival from the baseline value could make this technology a very cost-effective investment. Although additional evidence on this parameter is critical for assessing the economic value of potential diagnostic imaging systems, a clinical trial capable of showing such a small survival improvement would be very costly to conduct.

Figure 4 shows the detailed analysis of how two of the variables at a time affect the \$/LYG value. Since there are three crucial variables to examine, there are three combinations of two variables to look at. The first is how the cost-effectiveness varies as a function of both the Specificity and the cure rate. This chart confirms that a modest increase in cure rate (>1% above the current average) is necessary to achieve an acceptable cost effectiveness (<~ \$25,000/LYG) and if that is achieved, then basically any reasonable specificity will not invalidate the effectiveness of the device.

Figure 4b compares prevalence and cure rate and their effect on the \$/LYG. It demonstrates the region where the cost effectiveness becomes unacceptably high, which is when the prevalence is high, typically above 90%. In general, the prevalence can be high, or the cure rate could be low (close to 59%), but when they happen together, this is the worst case for cost effectiveness. From the graph, it can be seen that with only a marginal improvement in the cure rate and a prevalence of 90%, the bottom line is nearly \$80,000/LYG, but that number quickly decreases when either value improves.

In Fig. 4c, the prevalence and specificity are varied in the same graph, and the \$/LYG demonstrates a much more moderate effect on these parameters. Even when the prevalence is very high and the specificity is unrealistically low, the cost-effectiveness is not nearly as poor as in the previous example.

Discussion

The analysis presented in this paper assesses the economic potential for adopting imaging technology in the management of LABC for therapy decisions during neoadjuvant therapy. This analysis is important at this time, as the use of neoadjuvant therapy is in increasing use, and the number of devices undergoing pilot clinical trials is also increasing. Several key clinical trials have studied the issues related to the accuracy and sensitivity to change during neoadjuvant therapy, yet few have solid numbers about the specificity of the measurement. The rationale of accepting a new technology must be centered around the system having prognostic accuracy and also providing improved treatment outcome in a cost-effective manner. At the same time, improvements in routine NACT designs have come, and in the future, more specific treatments can be based upon genetic and clinical chemistry testing, which should provide a cure rate higher than the current national average of 59%.

In our analysis we used a willingness-to-pay threshold of \$25,000 per LYG as the criterion for establishing cost-effectiveness [21]. In this analysis, the precise threshold had little bearing on our findings. Instead, our focus was on characterizing the factors that most influenced the estimated cost-effectiveness of imaging. The graphs above isolate the most important assumptions and provide the caveat that the cure rate for the women who will ultimately fail NACT must be measurably higher than the 59% baseline used to characterize the current standard of care. Additionally, it is important that the initial response to standard NACT should not increase to above 90% if the diagnostic imaging is to be beneficial. However this latter issue is unlikely to be a problem, as there are clearly a group of patients who simply are not responsive to the existing standard NACT.

Interestingly these key parameters are values which are almost entirely dependent upon the disease and treatment efficacy, and to a greater extent less important was the imaging system characteristics. Thus, an important conclusion from this study is that the specificity and cost of the systems are not dominant factors in the cost effectiveness. While our initial calculations were looking at near-infrared imaging [16], the results of the study are applicable to a range of possible imaging systems that could be applied in the course of neoadjuvant therapy. This is important, because studies with ultrasound, PET and MRI have all been completed, and the cost and specificity of each of these systems varies considerably, yet each would likely have similarly acceptable cost effectiveness. It is likely that other issues such as access to the system will define if they have a role or not.

The largest uncertainty in this analysis left unanswered is to determine if switching a person from an ineffective therapy to another therapy would make sense as a clinical benefit, and if the time difference between switching early versus later in the treatment cycle is a factor. If the imaging test were shown to have prognostic value, it could be used to reduce the number of ineffective therapies given to those subjects who are not responding, and thereby minimize unnecessary morbidity and cost associated with continuing ineffective NACT. We note that our economic evaluation focused only on the cost of the imaging device and did not incorporate savings from ineffective therapy avoided. If non-responding subjects to initial NACT are identified early, the potential exists that the gain in treatment outcome could be substantial. Our analyses show that even if modest, any incremental benefit from switching to a more effective therapy could have substantial gains. These patients may have a measurable benefit from another type of chemotherapy, immunotherapy, or other emerging

combinations with hormonal therapies. One study examining the use of docetaxel based NACT in patients who failed to respond to anthracycline-based NACT showed that both clinical complete response and partial response rates were improved significantly with the addition of taxane based therapy, as compared to continuing eight cycles of an anthracycline based regimen [22]. While the benefit of earlier transition to a more effective chemotherapy regimen in any given patient is speculative at this point, it is not without reason to believe there would be some benefit.

Future clinical trials may focus on this aspect of changing therapy at an earlier versus a later time point in the treatment cycle. Additionally, this study did not examine how the timing of imaging affects cost-effectiveness. Some imaging modalities may provide truly prognostic data earlier or later in the treatment cycles. However much of the focus has been on developing systems that could provide useful data within the first weeks of the initial cycle, so there is less uncertainty about the timing than there is about other free parameters. Assessing how cost effectiveness may be altered by the timeline is an area that would merit further analysis with a specific imaging modality.

An additional parameter not discussed here is the actual cost of the therapy and how different therapies will actually have slightly different costs. Some therapies can induce further morbidity such as cardio-toxicity, and therefore even further increase cost per life year gained. As imaging advances, delineation in the types of neoadjuvant therapy would likely be beneficial.

Conclusions

As more information becomes available about the accuracy of diagnostic imaging of LABC and the efficacy of accelerated treatment that these women will receive, the cost effectiveness model presented here can be used to determine a more exact estimate of the device's cost effectiveness. At a willingness to pay threshold of \$25,000 per LYG, the cure rate should be at least 1% above the existing level to make prognostic imaging worthwhile, and the existing cure rate with standard chemotherapy would have to be below 90%. Additionally, the specificity of the device is unlikely to significantly limit the cost-effectiveness of prognostic imaging. Therefore based upon these analyses and the known limits of current chemotherapy, it appears as though most technologies to assess response to NACT early in the treatment cycle would be cost effective, if it could be shown that the treatment outcome was better for those patients shifted to a new therapy early in the treatment cycle. Future clinical trials need to focus on the question of whether there is a quantifiable benefit in shifting patients to more effective therapies, earlier in the cycle. However in order to carry out these clinical trials, imaging systems must be validated and used to determine accurately if patients are truly responding to the therapy or not.

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Fig. 1.

The schematic diagrams of patient flow with percentage values for each group are shown for (a) the current standard of care in neoadjuvant chemotherapy, (b) a possible patient flow with imaging intervention where the system was assumed to be perfect, and (c) intervention in the NACT with an imperfect imaging system, following all possible outcomes for subjects. This latter model was used in this study to analyze costs versus life years gained

Fig. 2. The cost per discounted life year gained (LYG) is shown for a single hospital or institution, based upon the number of new diagnoses per year

Fig. 3.

The sensitivity analysis graphs are shown plotting cost per life year gained (\$/LYG) versus some of the more important input values. In (a) the prevalence of people responding to the primary NACT was examined. In (b) the Life expectancy (LE) was varied as observed after a non-responding treatment of NACT. In (c) the specificity of the imaging system was varied, and in (d) the increase to the overall cure rate was varied based upon the imaging test and shift to secondary NACT affecting the outcomes

Fig. 4.

The sensitivity analysis is shown for variations in two input parameters at a time. In **(a)** the cure rate and specificity are examined, in **(b)** the prevalence and cure rate were varied, and in **(c)** the prevalence and specificity were varied. The plots indicated that varying combinations of the three parameters, cure rate, specificity and prevalence, can be combined to create excessively large values of \$/LYG, which would need to be avoided for useful imaging

Table 1

Base case parameters for the imaging modality and associated error rates

Parameter	Base case estimate (%)
Prevalence of cure	70
Sensitivity	70
Specificity	70
True negative	21
False positive	9
False negative	21
True positive	49

The input data from the Center for Disease Control (CDC) is listed for different age groups of women, including data of incidence of locally advanced breast cancer (LABC), estimation of Life Expectancy (LE), and the calculated discounted life years gained (LYG) from the treatment

Table 2

% Incidence by age	% of total	Average age at diagnosis	Life expectancy (LE) (non-responders)	Normal discounted LE (Responders)	LYG
0-30	0.045%	↔ 25	5	26.9	21.9
30s	0.380%	↔ 35	5	24.7	19.7
40s	1.426%	↔ 45	5	22	17
50s	2.496%	↔ 55	5	18.6	13.6
60s	2.795%	↔ 65	5	14.6	9.6
70s	2.857%	↔ 75	5	10.4	5.4
80s	2.500%	↔ 85	5	6.3	1.3
Total	12.5%	↔ Avg LYG/cured Pt. →			9.0

The population and age averaged value at the bottom was used as input to the model

Table 3

Base case results for a population of 213,000 women treated with prognostic imaging or standard care, based upon a case of 70% sensitivity and specificity

	Prognostic imaging	Standard care
Total population	213,000	213,000
True positive	104,370	n/a
TP cured	93,933	
TP deceased	10,437	
False negative	44,730	n/a
FN cured	40,257	
FN deceased	4,473	
False positive	19,170	n/a
FP cured	11,310	
FP deceased	7,860	
True negative	44,730	n/a
TN cured	27,285	
TN deceased	17,445	
Total cured	172,786	171,891
Total deceased	40,214	41,109