Prognostic imaging in neoadjuvant chemotherapy should be cost effective

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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. Predictive 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.

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]. In these pilot studies there is evidence that these biophysical changes occur within the first cycle of chemotherapy, 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. This study examines the range of performance characteristics required for imaging to provide a cost-effective means of tailoring NACT early in the treatment cycle.

Methods

The cost analysis was completed with respect to a generic imaging approach, such as could be done with US, PET, NIR or MRI. The computational flow model, as it was used, needed to include imperfect imaging systems, as is quantified by the sensitivity and specificity of the procedure. While these values are not clearly known, increasing numbers of false positives and negatives obviously would impact the cost effectiveness, and so a model to incorporate these parameters was created, and schematically shown in Figure 1. This model was used throughout this study to evaluate: 1) The medical benefit to these women for having this technology measured in terms of life years gained (LYG) and 2) the cost of providing this technology to them.

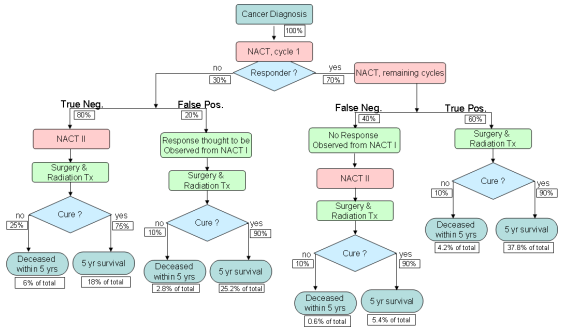

Figure 1. The computational flow model based upon neoadjuvant chemotherapy (NACT) and imaging during the first cycle to determine efficacy. Costs were assessed by assigning flow based upon the specificity of the imaging system and the expected outcomes for each path.

Results

Using a standard metric of $25,000 per discounted life year gained as a measure of a successful system, 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. 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.

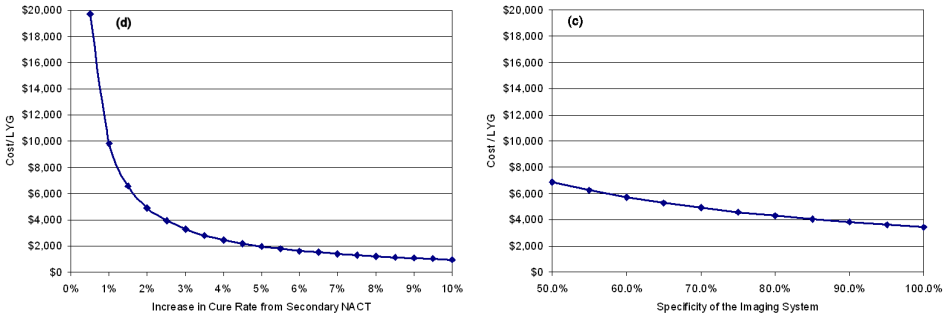

Figure 2. The cost per life year gained (Cost/LYG) is plotted for two of the more interesting parameters, including the increase in life sparing from the secondary chemotherapy (a), and the specificity of the imaging device (b).

Discussions

It can be concluded that at a cost-effectiveness of less than $25,000/ LYG, the cure rate should be at least 1% above the existing level to make this worthwhile. Additionally, the specificity of the imaging test is unlikely to significantly limit the cost-effectiveness. 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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