National Institute for Health and Care Excellence
Centre for Health Technology Evaluation

Pro-forma Response

Executable Model

INTRABEAM Photon Radiotherapy System for the adjuvant treatment of early or locally advanced breast cancer [ID618]

The economic model enclosed and its contents are confidential and are protected by intellectual property rights, which are owned by **Southampton Health Technology Assessment Centre (SHTAC), University of Southampton.** It has been sent to you for information only. It cannot be used for any other purpose than to inform your understanding of the appraisal. Accordingly, neither the model nor its contents should be divulged to anyone other than those individuals within your organisation who need to see to them to enable you to prepare your response. Those to whom you do show the documents must be advised they are bound by the terms of the Confidentiality Acknowledgement and Undertaking Form that has already been signed and returned to the Institute by your organisation.

You may not make copies of the file and you must delete the file from your records when the appraisal process, and any possible appeal, are complete. If asked, you must confirm to us in writing that you have done so. You may not publish it in whole or part, or use it to inform the development of other economic models.

The model must not be re-run for purposes other that the testing of its reliability.

Please set out your comments on reliability in writing providing separate justification, with supporting information, for each specific comment made. Where you have made an alteration to the model details of how this alteration was implemented in the model (e.g. in terms of programme code) must be given in sufficient detail to enable your changes to be replicated from the information provided. Please use the attached pro-forma to present your response.

Please prepare your response carefully. Responses which contain errors or are internally inconsistent (for example where we are unable to replicate the results claimed by implementing the changes said to have been made to the model) will be rejected without further consideration.

Results from amended versions of the model will only be accepted if their purpose is to test robustness and reliability of the economic model. Results calculated purely for the purpose of using alternative inputs will not be accepted.

No electronic versions of the economic model will be accepted with your response.

Responses should be provided in tabular format as suggested below (please add further tables if necessary).

April 2014

Issue 1

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
SHTAC draft and model emphasize 'recurrence' while the TARGIT-A randomised trial clearly shows that 'mortality' to be the outcome measure in the following health economic study.	a) Vaidya et al [1] have conducted a non-inferiority trial concluding that in terms of recurrence, the INTRABEAM treatment in **pre-pathology** stratum is not inferior to EBRT. Therefore, the main outcome measure of the health economic model is to be 'number of deaths' in both arms. b) Carl-Zeiss model based on this data [1] shows loss of LYGs/QALYs. c) SHTAC states that there is not sufficient information on the proportions of each type of recurrence and find it inappropriate to include the post-progression costs in the base case analysis. d) SHTAC's scenario analysis with assumptions and inclusion of post-progression costs shows an ICER of only 157 pounds per QALY lost. e) SHTAC model uses utility values from two different sources, COMICE trial and Lidgren et al [2, 3]. Use of model health state 'any other recurrence' and assigned low utility value are questionable.	Higher LYGs and QALYs are expected at the low INTRABEAM cost.

Issue 2

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
a) SHTAC draft states the fewer deaths in INTRABEAM arm are	a) Vaidya et al 2013 [1] have not given mean age of the populations in both arms rather age group wise	SHTAC's assumption of the lower death rate in the INTRABEAM group by chance

due to chance and due to 0.5 year younger mean age of the population in this arm.	included patients are shown in the web appendix e-table 1 and those are comparable in both arms. b) SHTAC ignores the fact that the whole breast radiation is associated with cardiac toxicity and ionizing radiations increase the subsequent rate of ischemic heart disease [4]. c) In the lead data source article by Vaidya et al [1] cardiac deaths in the whole breast radiation arm are four times higher than in INTRABEAM arm. d) Inclusion of deaths caused by ischemic bowel and stroke in the EBRT group would increase the death rate in this group to five and half times to the cardiovascular deaths in the INTRABEAM group.	is erroneous. Model emphasizing survival in both arms would show higher LYGs and QALYs for INTRABEAM.

Issue 3

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
Mastectomy in patients with local recurrence. SHTAC draft states that as per the clinical advice to AG mastectomy is a common practice after local recurrence.	In a model with 40 years' time horizon repeat lumpectomy could be considered for local recurrence (as in Carl-Zeiss model). Results from a large observational study of women with early breast cancer "provide confidence" that breast-conserving therapy is "an effective alternative" to mastectomy. Less invasive breast conserving therapy which is a combination of lumpectomy and radiation, provides better survival [5]. More women will be going for breast reconstruction because of better access to information. With surgical advances and increasing patient awareness towards treatment options and rising consciousness towards self-appearance and rebuilding of body image for self-confidence are likely to bring the change	Costs associated with mastectomy + reconstruction would be more appropriate for EBRT patients as conservative lumpectomy and breast conservation is not an option after whole breast irradiation. This may result in higher long term EBRT costs making INTRABEAM cost effective.

	in the practice of mastectomy [6].	

Issue 3

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
SHTAC: Following mastectomy, 50% patients opting for reconstruction.	Breast reconstruction has its benefits in body image, self-esteem, sexuality, and quality of life for the women traumatized by the breast cancer. Breast reconstruction has been shown to yield important psychosocial and quality of life benefits for patients with breast cancer that have undergone mastectomy [7-9]. Given the important psychosocial functions of the female breast in human society, breast reconstruction is a key consideration in the multidisciplinary management of breast cancer. As noted above in issue 3, the reconstruction figures are bound to increase in the coming years [10]. Relying on figures used in SHTAC model would be unrealistic to calculate the costs for next 40 years.	Mastectomy followed by reconstruction would increase the costs in EBRT arm significantly and will render it not cost effective.

Issue 4

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
SHTAC has done analysis from NHS perspective which is a norm in England. However, SHTAC draft recognizes the	The drawbacks of whole breast irradiation include cost, duration of treatment, lost productivity and inconvenience to	Keeping a 40 year time horizon, expected societal changes and societal demands in view, there is a need of incorporation of

impact of INTRABEAM use on the QoL of patients. It is also recognized that the use of INTRABEAM would reduce the productivity losses and would improve societal resources.	patients [11]. In a long term future analysis done for costs and consequences for 40 years, these facts can't be ignored. Evolving health care systems, changing patient's expectations and need to use every possible societal resource in an aging population need to be considered in an analysis spanning over four decades.	'other' costs in the analysis. We may have to think in the same way as we do for 'discounting' for future. Pure payer's perspective would not show realistic results for a time frame extending up to year 2054.

Issue 5

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
SHTAC draft states EAC of GBP 53,025.	The additional staff resources required for use (table 28) is less. Several additional hours are not needed in practice [expert opinion]. Also the additional time in the operating theatre is 30 minutes in average since sentinel lymph node evaluation is done at the same time.	INTRABEAM EAC and operating theatre costs are expected to be lower in the model.

Issue 6

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
Demand of INTRABEAM page 104-105, proportion of patient's suitable for	The demand taking into account the ASTRO suitable group is 31 % 2232. /. 708 [Vaidya et al]. Also the elderly population	Calculated costs per procedure are expected

INTRABEAM is 16 %.	suitable according to ASTRO with patients >= 60 is growing during the next 40 years. For cautionary / unsuitable patients INTRABEAM can be used as boost and increases the usage to 90 % of breast patients. A research abstract is submitted showing that INTRABEAM could be used for 30.1 % of all breast cancer patients [12].	to be lower as in table 33.

Issue 7

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
Relevance to NHS page 124 chapter 6 states 412 linear accelerators will be required by 2016.	The proportion of cases is more than 30 % with INTRABEAM an can free up the demand for the linear accelerators and therefore save higher investment costs for the LINACS. Also with the growing elderly population patients above 60 can be treated with INTRABEAM and save LINAC slots. Moreover, researchers have voiced the need for change in practices based on evidence and move forward with adopting safe new treatments in order to make them available to the patients in need [13].	The need for additional investments for linear accelerators is expected to increase the costs for the standard EBRT therapy.

References

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