

Institution: University of Surrey
Unit of Assessment: UOA 15 General Engineering
Title of case study: Modelling of Cancer Treatment
<p>1. Summary of the impact</p> <p>Research conducted at the University of Surrey has resulted in a suite of clinically-relevant, multi-scale mathematical models being developed and used within the NHS [1-3].</p> <p>One of these models, MALTHUS, now funded by the National Cancer Action Team, predicts demand for radiotherapy across England and Wales. MALTHUS is a national metric and NHS commissioners are required to use MALTHUS to justify purchases of new radiotherapy equipment. Ipswich was the first to use Malthus in evidence to justify successfully the purchase of new equipment.</p>
<p>2. Underpinning research</p> <p>Radiotherapy (RT) is a highly effective cancer treatment, medically and economically, being responsible for success in 40% of patients cured of cancer (compared to 49% for surgery and 11% for drug treatment) [1-4]. In the past two years, there has been a complete revolution in the way the NHS proposes to commission services. GP commissioning of cancer services has now been abandoned in favour of central commissioning by the Radiotherapy Clinical Reference Group operating within the NHS Improving Quality initiative. It is therefore important and timely that a tool exists to predict accurately the future demand for radiotherapy regionally and nationally.</p> <p>A course of RT is delivered as a series of 'fractions' usually daily over a number of weeks. In a simple treatment, the dose per fraction and the target volume are constant but in more complicated treatments both can be varied. Concomitant and adjuvant chemotherapy can also be given to enhance the effectiveness of the RT and we have developed multi-scale models to help clinicians understand the complicated interactions between chemo- and radio-therapy [1-3].</p> <p>The MALTHUS (Monte Carlo Application for Local Treatment and Healthcare Usage Simulation) model developed at Surrey predicts demand for radiotherapy due to all types of cancer [5-6]. It uses clinical decision trees obtained from the published evidence base and by questioning groups of leading clinicians. The program can then launch a population of virtual patients with representative age and sex distributions, socio-economic characteristics and cancer disease incidence, through these trees to predict the demand for radiotherapy equipment.</p> <p>Malthus is a close collaboration between the clinicians in Cambridge and the modelling expertise at Surrey where a research version of the program is under continuous development to provide state of the art tools not normally exploited in the NHS. The modelling and solution algorithms originate from Surrey, whilst Cambridge provides the clinical decision trees.</p> <p>Data for cancer incidence is supplied by the regional cancer registries via the National Cancer Intelligence Network (NCIN), and population statistics and predictions are supplied by the Office for National Statistics (ONS). The model constructs representative populations of patients which are then fed to a discrete event simulation of the clinical decision processes in the form of a binary decision tree. This process is effectively a Monte Carlo integration over all possible clinical pathways. Each virtual patient collects a virtual patient record as they pass through the tree, and once a cohort has been 'treated', the number of RT fractions is summed. This cohort calculation process is embedded in a Monte Carlo simulation in order to predict the effects of uncertainty in</p>

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the population and incidence data and the parameters of the clinical decision trees. Hence users of the program can be supplied with both the expected number of fractions for the chosen cohort and the likely errors in this estimate.

An important feature of this methodology is that it has the capacity to be extended to predict, for instance, the demand for complex RT and the theatre time required due to surgery.

3. References to the research

1. Kirkby, N.F., Jefferies, S.J., Jena, R., and Burnet, N.G., 'A mathematical model of the treatment and survival of patients with high-grade brain tumours', *Journal of Theoretical Biology*, **245** (1), pp 112-124, 2007
2. Burnet, N.G., Jena, R., Jefferies, S.J., Stenning, S.P., Kirkby, N.F., 'Mathematical modelling of survival of glioblastoma patients suggests a role for radiotherapy dose escalation and predicts poorer outcome following delay to start treatment', *Clin. Onc.*, **18** (2), pp 93-103, 2006
3. Barazzuol, L., Burnet, N.G., Jena R, Jones, B., Jefferies, S., & Kirkby, N.F., 'A mathematical model of brain tumour response to radiotherapy and chemotherapy considering radiobiological aspects', *Journal of Theoretical Biology*, 262(3), pp553-565, 2010.
4. Burnet, N.G., Jefferies, S.J., Benson, R.J., Hunt, D.P., & Treasure, F.P. , 'Years of life lost (YLL) from cancer is an important measure of population burden--and should be considered when allocating research funds', *Br J Cancer*, 92(2), pp241-5, 2005.
5. Round CE, Williams MV, Jena R, Mee T, Kirkby NF, Cooper T, Hoskin P. (2013) 'Radiotherapy Demand and Activity in England 2006-2020'. *Clin. Onc.*, doi: 10.1016/j.clon.2013.05.005
6. Round C, Williams MV, Jena R, Mee T, Kirkby NF, Cooper T. (2013) 'The Malthus Programme: Developing Radiotherapy Demand Models for Breast and Prostate Cancer at the Local, Regional and National Level'. *Clin. Onc.*, doi: 10.1016/j.clon.2013.05.006

4. Details of the impact

A BBSRC/EPSRC/MRC-funded "discipline hop" enabled Professor Norman Kirkby from the University of Surrey's Chemical & Process Engineering Department to spend a year at the Oncology Centre in the Addenbrooke's Hospital, Cambridge. As a direct result of this opportunity a suite of multi-scale mathematical models have been generated which go from the cellular level right through to national policy and decision-making level [1]. One resulting paper has been a highly cited publication [2 above]. A consultant neuro-oncologist from the Addenbrookes is now seconded to Chemical & Process Engineering at Surrey for one day a fortnight; this arrangement is unique in the UK and critical to ensuring that the research has a full reach 'from bench to bedside'.

One of these models, **MALTHUS** (Monte Carlo Application for Local Treatment and Healthcare Usage Simulation) commissioned by the National Cancer Action Team (NCAT) is available as a download so that clinicians and commissioners can plan current and future radiotherapy demand for their network or region. As of March 2013, MALTHUS had over 100 users; however it is now incorporated in the "standard PC build" for a number of NHS trusts and so the exact number of users is unknown. The first use of MALTHUS to justify purchase of new equipment was made by Ipswich using the beta release version.

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MALTHUS was originally developed for England but has been extended to Wales and recently the program has been made available to research groups in Scotland, Australia and Canada. The European Society for Radiotherapy and Oncology is considering MALTHUS for incorporation into their Health Economics in Radiation Oncology Project [2].

One unique feature of this program is that we have achieved a national consensus on best RT practice. MALTHUS is also being used by clinicians because it contains a repository of this evidence base. The decision trees in MALTHUS are now also used to assess clinical performance in RT departments

The government has recently announced volcanic changes to the way NHS commissioning will operate; it has never been more important to have robust and reliable tools to predict demand for services. The long-term benefit of MALTHUS is that it represents a nationally-agreed, systematic way of deciding how many fractions of radiotherapy are likely to be required in any given location and thereby will remove the 'postcode lottery'.

The impact of Surrey's research is well illustrated by stake holder feedback, a selection is included below;

In his letter to the Cancer Network Directors, January 2012 [3], the National Cancer Director, said (our underline):

“... the new Malthus modelling tool for radiotherapy demand. This tool uses evidence-based radiotherapy decision trees based on UK clinical practice and local cancer incidence data. From this it calculates radiotherapy demand requirements and can model forward to take account of changes in cancer incidence as the population ages. This is likely to produce a more realistic model for radiotherapy demand than the NRAG model and I have no doubt will be a focus of your radiotherapy plans into the future...” Later in the letter he added: ***“I would encourage you and your colleagues to use this model regularly and update the version in use.”*** And, ***“I would therefore encourage commissioners to use the Malthus tool for radiotherapy planning... These results should be used to inform strong commissioning discussions with providers.”***

In the Department of Health report; Radiotherapy in England 2012” [4] :

“To support accurate workforce planning the outputs from Malthus are being used to feed the development of a workforce planning tool for the physics and radiography workforce (the Workforce Integrated Planning Tool, WIPT). This will help identify the overall requirements for national training numbers for the physics and radiographic professional groups taking account of emerging changes to local skill mix as a result of new techniques and technologies”

For lung cancer (~1300 avoidable deaths per annum if survival in England is matched to the best in Europe [5]) the DoH [4] in 2012 added

“Lung cancer fractionation is much more diverse because the intent of treatment may be palliative or radical. A significant proportion of patients receive short palliative regimens, all of which are supported by clinical trial evidence in different settings. Radical treatment is dominated by 20 fraction regimens which have a poor evidence base. Few patients receive treatment in 30 or more fractions which would be standard in most of Europe and North America for many indications. This should be addressed in the commissioning process through use of the evidence based decision trees in the Malthus model.”

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An overview of radiotherapy services from the NHS National Cancer Action team [6], guidance on the management of radiotherapy capacity from the Royal College of Radiologists [7] and the NHS standard contract for radiotherapy [8] each demonstrate that Malthus is now embedded as a standard and important tool for the planning and management of radiotherapy services throughout the UK.

The Malthus web site is publicly accessible and provides further illustrations of the impact achieved [9]

5. Sources to corroborate the impact

1. Jena, R., Round, C., Mee, T., Kirkby, N., Hoskin, P. & Williams, M., 'The Malthus Programme – A New Tool for Estimating Radiotherapy Demand at a Local Level', Clin. Onc., 24, pp1-3, 2012.
2. ESTRO HERO project web site <http://www.estro.org/about/health-economics-in-radiation-oncology---hero/hero>
3. <http://www.sor.org/news/radiotherapy-services-modelling-tool> This link includes a download for the letter from the National Cancer Director to all NHS Network Directors, dated 16th January 2012.
4. Department of Health, "Radiotherapy Services in England 2012" <https://www.gov.uk/government/publications/radiotherapy-services-in-england-2012>
5. Tim Cooper NCAT presentation to North Trent Cancer Network on Modelling Radiotherapy <http://www.northtrentcancernetwork.nhs.uk/professionals/workshop---14th-june-2011.htm>
6. National Cancer action Team Delivering world class radiotherapy <http://www.radpro.eu/radproexpo2012/ncat/ncat.html>
7. Guidance on the management and governance of additional radiotherapy capacity <http://www.ipem.ac.uk/Portals/0/Documents/Publications/Guidance%20on%20the%20Mgt%20and%20Governance%20of%20additional%20RT%20capacity%202013.pdf>
8. 2013/14 NHS England Standard contract for Radiotherapy <http://www.england.nhs.uk/wp-content/uploads/2013/06/b01-radiotherapy.pdf>
9. Malthus web site <http://www.camradiotherapy.org.uk/malthus>