



## Original Article

# Variations in Demand across England for the Magnetic Resonance-Linac Technology, Simulated Utilising Local-level Demographic and Cancer Data in the Malthus Project

T. Mee<sup>\*†</sup>, A.J. Vickers<sup>\*†</sup>, R. Jena<sup>‡</sup>, K.J. Kirkby<sup>\*†</sup>, A. Choudhury<sup>\*†</sup>, N.F. Kirkby<sup>\*†</sup>

<sup>\*</sup> Division of Cancer Sciences, School of Medical Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

<sup>†</sup> The Christie NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK

<sup>‡</sup> University of Cambridge Department of Oncology, Cambridge Biomedical Campus, Addenbrooke's Hospital, Cambridge, UK

## Abstract

**Aims:** Cancer incidence varies across England, which affects the local-level demand for treatments. The magnetic resonance-linac (MR-linac) is a new radiotherapy technology that combines imaging and treatment. Here we model the demand and demand variations for the MR-linac across England.

**Materials and methods:** Initial clinical indications were provided by the MR-linac consortium and introduced into the Malthus radiotherapy clinical decision trees. The Malthus model contains Clinical Commissioning Group (CCG) population, cancer incidence and stage presentation data (for lung and prostate) and simulated the demand for the MR-linac for all CCGs and Radiotherapy Operational Delivery Networks (RODN) across England.

**Results:** Based on the initial target clinical indications, the MR-linac could service 16% of England's fraction burden. The simulated fractions/million population demand/annum varies between 3000 and 10 600 fractions/million at the CCG level. Focussing only on the cancer population, the simulated fractions/1000 cancer cases demand/annum ranges from 1028 to 1195 fractions/1000 cases. If a national average for fractions/million demand was then used, at the RODN level, the variation from actual annual demand ranges from an overestimation of 8400 fractions to an underestimation of 5800 fractions. When using the national average fractions/1000 cases, the RODN demand varies from an overestimation of 3200 fractions to an underestimation of 3000 fractions.

**Conclusions:** Planning cancer services is complex due to regional variations in cancer burden. The variations in simulated demand of the MR-linac highlight the requirement to use local-level data when planning to introduce a new technology.

© 2021 The Royal College of Radiologists. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Key words:** Demand modelling; health services needs and demand; health services research; MR-linac; radiotherapy; Radiotherapy Operational Delivery Network

## Introduction

Cancer is a leading cause of mortality, in both the UK and worldwide, with 367 167 new diagnoses in the UK every year (2015–2017) [1]. Incidence rates have increased by 7% in the past decade [1] and the number of cases is predicted to rise by a further 1.6%/year until 2035 [2]. Cancer survival is also increasing, and has doubled in the past 40 years, with an estimated 50% of patients diagnosed with cancer in the UK now surviving for over 10 years [3]. This is largely due to successful advances in our ability to

diagnose and treat the disease [4]. It is estimated that about 40% of patients who are cured of their disease have a treatment that includes radiotherapy [5]. However, reports in 2007 [6], 2012 [7] and 2014 [8] indicated that provision of radiotherapy in the UK falls short of demand [6,9]. Initiatives and models have been introduced in an attempt to quantify the gap between current levels of conventional radiotherapy provision and estimated demand at both a national [10,11] and local level. One mathematical model currently being used for both national and local-level radiotherapy demand simulations is the Malthus model [12]. Previous work has shown the importance of accounting for local variations in demand [13,14]. Malthus outputs showed about a three- and five-fold variation in local-level demand in terms of fractions/head of population for breast and prostate cancer, respectively [13].

Author for correspondence: T. Mee, 3.08 3<sup>rd</sup> Floor, Proton Beam Centre, The Christie NHS Foundation Trust, Wilmslow Road, Manchester M20 4BX, UK.

E-mail address: [thomas.mee@manchester.ac.uk](mailto:thomas.mee@manchester.ac.uk) (T. Mee).

As well as increasing the provision of conventional radiotherapy treatments, there has been increased utilisation of advanced radiotherapy modalities, including image-guided radiotherapy, intensity-modulated radiotherapy and proton beam therapy [15,16]. A common goal is increasing the number of adaptive radiotherapy treatments, defined as ‘aiming to customise each patient’s treatment plan to patient-specific variation by evaluating and characterizing the systematic and random variations through image feedback and including them in adaptive planning’ [17]. One attempt to achieve this is the development of simultaneous magnetic resonance imaging (MRI) and radiotherapy treatment delivery [18]. Examples include the MRIdian [19] (ViewRay, Cleveland, Ohio, USA), the Australian MR-linac system [20], the Linac-MR [21] (University of Alberta, Canada) and the Unity MR-linac system developed by Elekta (Stockholm, Sweden) and Philips (Amsterdam, the Netherlands) in partnership with The University Medical Centre, Utrecht [22]. At the time of writing, in England there are two Unity machines in operation, one at The Christie NHS Foundation Trust and one at The Royal Marsden NHS Foundation Trust, and one MRIdian at GenesisCare Oxford.

Technically, the MR-linac could be used to treat any current clinical radiotherapy indication. However, the MR-linac is more expensive than a conventional linac (£5 million [23] versus £1.6 million [24]). Therefore, the clinical target must be carefully selected for maximum impact. In times of budget limitations and demand for return on investment, it is important that any new technology or treatments should be introduced in a cost-effective manner [25–27]. This may be achieved by ensuring that facilities and resources are distributed to maximise their utility. It is important to identify specific regions within a country where there is the demand for the technology and the infrastructure is in place to deliver it. Predicting local demand for nascent services and prioritising high-quality local data above nationally averaged data is one way to accomplish this aim.

Here we aim to determine and show the variation in regional demand for the MR-linac system to aid the implementation of the technology and maximise both its utility and cost-effectiveness. This will be achieved by encoding consensual clinical indications, provided by the MR-linac consortium [28], into the Malthus model [12].

## Materials and Methods

This study adapted the existing evidence-based clinical decision trees (CDTs) in the Malthus model [13] with the addition of some consensus-derived indications for the MR-linac. Although papers, such as Corradini *et al.* [29], have presented the potential initial applicability of a MR-guided radiotherapy solution across a broad range of different clinical sites, the clinical indications used for this study were determined by the MR-linac consortium in conjunction with international experts [30] and are shown in Table 1. The MR-linac consortium was formed in 2012 and consisted of seven international institutes installing clinical

prototypes of Elekta’s MR-linac and technical partners. The member base included radiation oncologists, physicists, technologists, engineers, dosimetrists, radiation therapists, researchers, epidemiologists, radiographers and statisticians. The clinical indications were selected through the collaboration of the whole consortium and were based on expected clinical benefits, such as increased local control, decreased toxicity and a better quality of life [30].

The existing Malthus CDTs contain around 2000 evidence-based clinical decisions relating to conventional radiotherapy [32]. The introduction of MR-linac treatment indications impacted on six CDTs – prostate, central nervous system, head and neck, non-small cell lung cancer, oesophagus and pancreas (see Table 1).

Most of the MR-linac indications align with current stage-based radiotherapy indications included in Malthus, such that an entire stage grouping or treatment indication could be remapped from conventional radiotherapy to an MR-linac indication. Where divergence occurred from the current CDTs, new data were sourced, as indicated below, to ensure the appropriate proportions of patients were allocated to the new MR-linac indications. Specifically, Malthus separates glioma into low grade (I and II) and high grade (III and IV), whereas the MR-linac target indications are grade II, III and IV gliomas. Here we sourced data from published literature [31], with input from clinicians with expertise in this area to estimate the proportion of low-grade gliomas that are grade II. For the main simulations, we assumed that the MR-linac indications for all cancer sites would be treated with the same numbers of fractions as conventional radiotherapy.

Given the utility of the MR-linac for the implementation of hypofractionation, but current lack of clinical evidence, we will use two hypothetical examples of hypofractionation to show the effect it may have on the demand for the MR-linac. We will simulate the effects of 15-fraction hypofractionation in stage III lung cancer [33] and three-fraction extreme-hypofractionation in intermediate-risk prostate cancer [34]. We have assumed that if a patient is eligible to receive radical radiotherapy they are also eligible to receive hypofractionated radiotherapy. Therefore, for the hypofractionation trial we will simply change the conventional number of fractions to the hypofractionated number.

The Malthus model has been previously described [12,35]. In brief, Malthus routes a population of virtual cancer patients, which are representative of the demographics and incidence profile in the region being simulated, through the relevant disease-specific CDTs. The CDTs are based on evidence gathered from guidelines, clinical trials, registry data, national consensus and expert opinion. The Malthus model CDT evidence base closely aligns with the Royal College of Radiologists’ dose fractionation document [36]. Malthus collects information on how many virtual patients were prescribed radiotherapy (either conventional or MR-linac) and the number of fractions prescribed during a simulation. The virtual patients traverse through the CDTs in a Monte-Carlo integration, undertaking 1 000 000 walkthroughs to ensure every clinical decision is adequately represented and the averages

**Table 1**

Magnetic resonance-linac (MR-linac) clinical indications [28] and the location of the radical radiotherapy indications within the Malthus clinical decision trees (CDTs) converted to MR-linac indications, with specific information on adjustments made

MR-linac clinical indication	Malthus cancer site	Malthus stage group	Malthus CDT branch	Adjustments to select subgroup and data source
Stage III non-small cell lung cancer	Non-small cell lung cancer	Stage 3a	Surgery – positive margin	–
		Stage 3b	No surgery – definitive radiotherapy Good performance status – radiotherapy	–
Intermediate risk prostate cancer	Prostate	Intermediate risk	Radical radiotherapy	–
T1–2, N0–2a, small volume in n2b, low risk human papilloma virus positive oropharyngeal cancer	Head and neck – oropharynx	Stage I–II Stage III–IV	Fit for curative Stage III–IVB – fit for curative	– Data taken from Christie database, 47% of stage III–IVB are eligible
Grade II, III, IV gliomas (eligible to receive standard fractionated radiotherapy [60 Gy/30 or 59.4 Gy/33] with concurrent temozolomide)	Central nervous system	High grade glioma Low grade glioma	Radical	– 8% of low grade reduced to 6.6% for grade II only (low = I+II) [31]
Locally advanced pancreatic cancer	Pancreas	Stage I Stage II	Non-resectable Non-resectable	– Data taken from Christie database, 36% [2016] –40% [all years] of stage II eligible
		Stage III	Non-resectable	Data taken from Christie database, 38% [2016] –48% [all years] of stage III eligible
		Stage I Stage II	Radiotherapy All radical radiotherapy indications	– –
cT2–4N0/cTxN1–3M0 oesophageal cancer	Oesophageal	Stage III	All radical radiotherapy indications	–

from the walkthroughs taken. Data for each Clinical Commissioning Group (CCG) and cancer site have been collected to show the number of patients eligible for treatment on the MR-linac.

An initial piece of scoping work testing the suitability of using Malthus for MR-linac indications was undertaken by Sanderson *et al.* [37] in a single region in England for lung cancer and prostate cancer. Here, Malthus was used to create a statistically representative cohort of virtual cancer patients for every CCG within England, and also for England itself, for the year 2019. This used CCG-level incidence projections of individual cancer sites [2] and the Office for National Statistics sub-national population projections [38]. CCG-level stage presentation data were included for lung and prostate cancer [39] and 3 years of data were used (2013–2015) [40]. There were no stage data for central nervous system and head and neck tumours available at the

CCG level. Likewise, the levels of incomplete data and unstaged data were also too high for oesophagus and pancreas to enable accurate forecasts at the CCG level, so the national averages were used.

Given the cost and lack of clinical experience of the MR-linac, implementation strategies should focus on the establishment of a supra-regional network of machines, such that patients travel to the nearest comprehensive centre to access treatment. In England, the new Radiotherapy Operational Delivery Networks (RODN) [41] are prime candidates for these regional networks. RODNs are formed from existing cancer networks. Table 2 shows which cancer alliance(s) contribute to each RODN. Each RODN contains at least one large tertiary centre capable of delivering a comprehensive cancer service. CCG boundaries [42] on the resulting heat maps [43] do not include the most recent boundary change between NHS Cumbria CCG and

NHS North Lancashire CCG, forming NHS Morecambe Bay CCG and NHS North Cumbria CCG. Consequently, we have assumed that the RODN boundary in the North West (between 9 and 11) also does not contain this boundary change.

## Results

Overall, the simulation estimates that 4.2% of England's cancer patients would be eligible for treatment on the MR-linac, based on the initial clinical indications provided by the consortium. This is in the context of a total predicted appropriate rate of radiotherapy utilisation (ARR), which is the percentage of simulated patients requiring radiotherapy treatment, of 40.5% (excluding retreatments) (see [Table 3](#)).

If standard fractionation schemes are applied, the MR-linac is simulated to be eligible for up to 16% of the simulated fraction burden for England. The total number of fractions simulated for the MR-linac (MR-linac fractions) is about 351 000, with lung and prostate treatments accounting for over 60% of that figure. [Table 3](#) shows the number of fractions for the cancer sites relevant to the MR-linac and the contribution to the overall simulated fraction burden of that cancer site.

[Figure 1](#) shows the number of standard-scheme MR-linac fractions and the number of fractions simulated for the MR-linac/million population for each CCG on a map of England. [Figure 2](#) shows the number of MR-linac fractions and fractions/million population simulated for each RODN on a map of England.

Due to the variations in cancer stage presentation and overall differences in case-mix across England, the simulated MR-linac fractions/million virtual population/year ranges from 3000 up to 10 600 fractions/million at the CCG level. Focussing only on the cancer population, the simulated MR-linac fractions/1000 cancer cases ranges from 1028 up to 1195 fractions/1000 cases. At the RODN level, the simulated fraction demand ranges from 13 700 up to 48 200 fractions. The number of simulated MR-linac patients ranges from 520 up to 1750/network. Due to the heterogeneity of the population within England, two regions with a very similar percentage of eligible patients may not have the same MR-linac fraction demand. There are 21 CCGs with an MR-linac ARR of 4.0%, but across those 21 CCGs the fractions/million demand for the MR-linac varies from 3500 to 8600 fractions/million. These observations are consistent with previous applications of our model.

[Table 2](#) has grouped the results into the 11 RODNs of NHS England. The table highlights the over- or under-prediction of demand if the average MR-linac fractions/million and fractions/1000 cases for England is applied to the RODNs without using any local-level data. The largest differences between a local-level simulation for a RODN and what the estimated demand if the national average fractions/million is used were an overestimation of 8400 fractions for RODN 1 and 2 and an underestimation of 5800 fractions for RODN 9. When using the national average fractions/1000 cases, RODN 1 has an overestimation of 3200 fractions and RODN 6 an underestimation of 3000 fractions.

[Table 4](#) shows the effects of two hypothetical examples of hypofractionation that could apply to the MR-linac. If hypofractionation schemes are applied to stage III lung and intermediate-risk prostate cancer, the simulated fraction demand for the MR-linac accounts for 11% of the simulated fraction burden for England. Compared with standard fractionation schemes, the simulated demand would drop from 107 400 to 49 900 fractions for lung cancer and from 112 100 to 16 800 fractions for prostate cancer. The total number of MR-linac fractions decreases by about 45% from 351 000 to 198 200 fractions. The number of patients would remain the same.

## Discussion

There are variations in cancer incidence across the country, including variations in the case-mix and stage at presentation, and these variations affect the local demand for cancer services. When planning to introduce a new technology into cancer services, the local-level demand should be taken into account. If the introduction of a new technology occurs where demand is too low, there could be insufficient patients for an adequate economic evaluation. There are research tools available, with granular cancer incidence and population data, that can model the local-level demand for radiotherapy. Although there are a few radiotherapy demand models available [[10,11](#)], here we show the use of the Malthus model to estimate the national demand and to quantify regional variations in demand for the MR-linac. This was achieved by modifying the current clinical evidence base of Malthus to include new target MR-linac indications for radiotherapy.

The target clinical indications chosen are not a definitive list of potential indications for any form of MR-guided radiotherapy. The clinical indications in this study were chosen as the MR-linac consortium has working groups focussing on those disease sites. Therefore, there is active research in those areas and specific indications could be provided to include in the modelling. The addition or removal of clinical indications could have a large influence on the potential demand, depending on both the target cancer site and the number of fractions. The removal of the prostate clinical indication in this study would reduce the number of patients by about 42%. This shows that the right balance must be struck between target clinical indication to achieve outcomes and health economic analysis to determine cost-effectiveness. By utilising a pre-existing model, such as Malthus, scenarios can be run to estimate the impact of changing clinical indications without creating a new demand model every time.

Malthus simulated the demand for the MR-linac at the national, RODN and CCG level. It estimated that 4.2% of all cancer patients could be eligible for this treatment. This translates to around 16% of the entire fraction demand across England. The fraction demand reduces to 11% with hypothetical examples of hypofractionation for stage III lung and intermediate-risk prostate cancer. Although

**Table 2**

Total simulated magnetic resonance-linac (MR-linac) fractions in the Radiotherapy Operational Delivery Networks (RODN) within NHS England (also showing the respective cancer alliances covered [40]), the population, the number of cancer cases and simulated MR-linac cases in each network. Also shown is the difference in a region's simulate demand if England's average demand figures were used in place of local-level data

RODN Number	Cancer alliance(s)	Population	Cancer cases	Simulated MR-linac patients	Simulated MR-linac fractions	Fractions/million population				Fractions/1000 cancer cases			
						MR-linac fractions/million	MR-linac fractions if England average used	Difference between local-level simulation and if England average is used		MR-linac fractions/1000 cases	MR-linac fractions if England average used	Difference between local-level simulation and if England average is used	
1	North West and South West London	6 772 300	32 245	1280	33 815	4993	42 201	8387	(+25%)	1017	36 997	3183	(+9%)
2	Surrey and Sussex	3 550 100	12 435	516	13 698	3858	22 122	8424	(+61%)	1102	13 838	141	(+1%)
3	North Central and North East London	3 692 500	17 777	752	19 788	5359	23 010	3222	(+16%)	1113	19 783	−4	(0%)
4	South East London	3 692 500	17 777	752	19 788	5359	23 010	3222	(+16%)	1113	19 783	−4	(0%)
4	Kent and Medway Peninsula	4 584 800	29 762	1173	30 599	6674	28 570	−2029	(−7%)	1028	33 121	2522	(+8%)
5	Somerset, Wiltshire, Avon and Gloucestershire	4 584 800	29 762	1173	30 599	6674	28 570	−2029	(−7%)	1028	33 121	2522	(+8%)
5	Thames Valley	5 000 100	29 252	1187	30 830	6166	31 158	328	(+6%)	1054	32 554	1724	(+6%)
6	Wessex	5 000 100	29 252	1187	30 830	6166	31 158	328	(+6%)	1054	32 554	1724	(+6%)
6	East of England	6 559 700	37 109	1751	44 354	6762	40 877	−3477	(−8%)	1195	41 297	−3056	(−7%)
7	East Midlands	4 214 600	24 228	1017	26 893	6381	26 263	−630	(0%)	1110	26 962	69	0%
8	West Midlands	5 861 500	33 254	1470	38 369	6546	36 526	−1843	(−5%)	1154	37 007	−1362	(−4%)
9	Lancashire and South Cumbria	6 801 300	41 109	1754	48 244	7093	42 382	−5862	(−12%)	1174	45 749	−2495	(−5%)
10	Greater Manchester	6 801 300	41 109	1754	48 244	7093	42 382	−5862	(−12%)	1174	45 749	−2495	(−5%)
10	Cheshire and Merseyside	6 801 300	41 109	1754	48 244	7093	42 382	−5862	(−12%)	1174	45 749	−2495	(−5%)
10	Humber, Coast and Vale	5 850 400	34 797	1397	38 238	6536	36 457	−1782	(−5%)	1099	38 724	486	(+1%)
10	West Yorkshire	5 850 400	34 797	1397	38 238	6536	36 457	−1782	(−5%)	1099	38 724	486	(+1%)
10	South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	5 850 400	34 797	1397	38 238	6536	36 457	−1782	(−5%)	1099	38 724	486	(+1%)
11	North East and Cumbria	3 313 700	21 729	931	25 389	7662	20 649	−4740	(−19%)	1168	24 181	−1208	(−5%)
England		56 201 000	313 697	13 210	350 215	6231	N/A	N/A	N/A	1113	N/A	N/A	N/A

**Table 3**

Simulation results for standard fractionation schemes showing the magnetic resonance–linac (MR–linac) targeted six cancer sites, and the figure for all cancers for comparison with the total radiotherapy demand, extracted from a simulation of England (2019) covering all of the Malthus 23 cancer groups

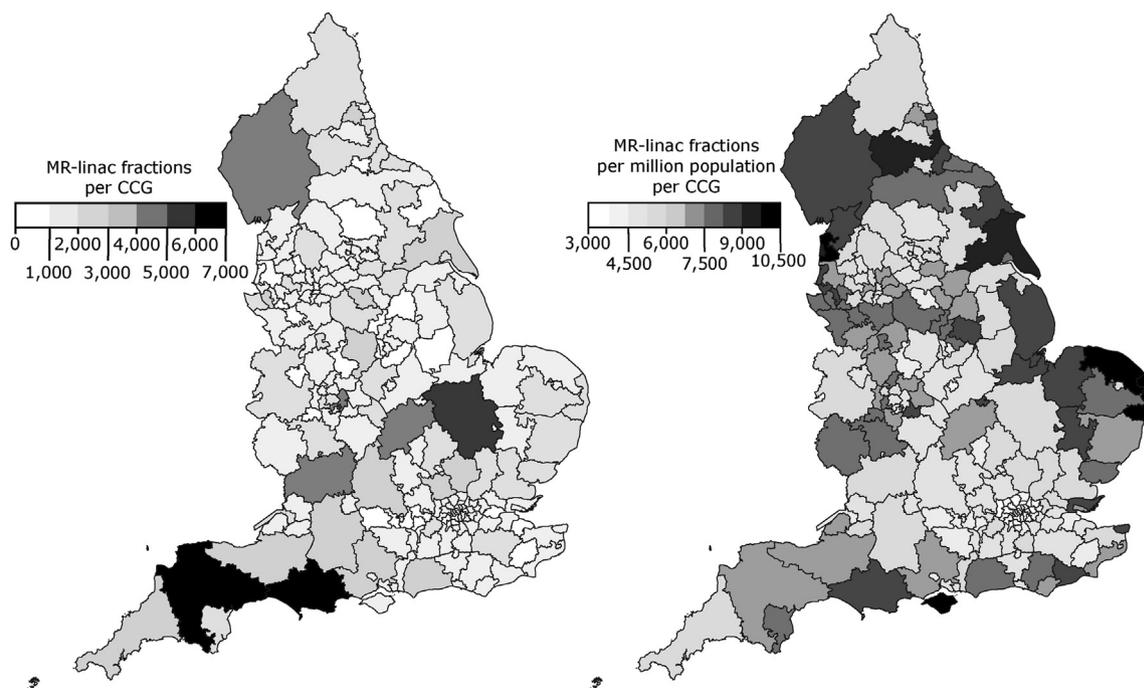
Cancer site	Appropriate rate of radiotherapy	% patients receiving conventional radiotherapy	% patients receiving MR–linac	Average fractions/MR–linac patient	Total MR–linac fractions	MR–linac fractions as % of all fractions for cancer site
Central nervous system	68%	34%	34%	29.6	46 000	65%
Head and neck	81%	68%	13%	34.2	46 300	17%
Lung	61%	52%	9%	32.3	107 400	36%
Oesophagus	30%	15%	15%	27.3	31 600	84%
Pancreas	15%	12%	3%	28	7600	34%
Prostate	51%	37%	13%	20	112 100	29%
All cancer sites	40.5%	36.3%	4.2%	–	351 000	16%

hypofractionation will be a significant part of the clinical utility of the MR–linac, there is currently a lack of consensus and efficacy data on appropriate hypofractionation for each treatment indication. Therefore, although the access rate figures and simulated patient numbers are probably accurate, the fraction demand figures should be considered as an upper limit of fraction burden.

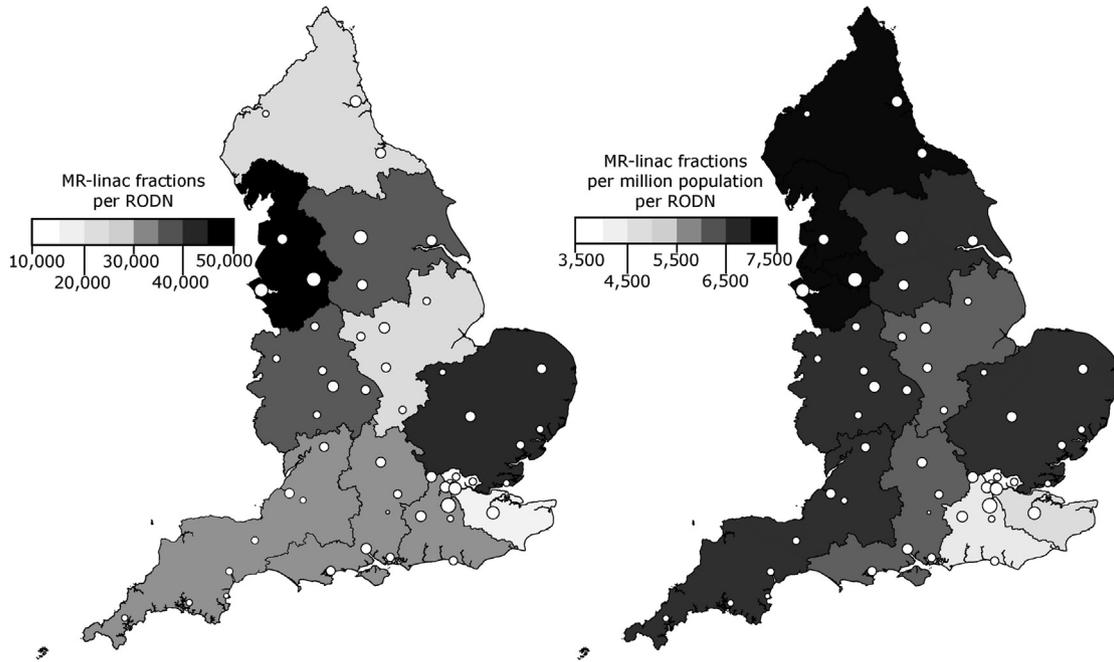
The fraction demand percentage is noticeably higher than the percentage of eligible patients because the target MR–linac indications used in this study are for radical intent only. However, the simulations will evolve and the numbers updated as evidence is generated or hypothesised for novel clinical MR–linac indications. For example, one potential MR–linac target that could increase the patient numbers to a greater extent than the fraction burden is oligometastatic disease.

The estimated demand for the MR–linac does vary across England, due to the regional variations in overall cancer burden, cancer case mix and stage at presentation. For the MR–linac, the initial lung and prostate clinical indications targeted only a limited stage/risk and therefore the local-level stage at presentation has a strong effect on demand. The overall patient demand ranges from 3% of CCG cancer incidences up to 6% and the fractions/million demand ranges from 3000 up to 10 600. When analysing simulated fraction demand as a proportion of cancer cases, the difference in demand is less marked, ranging from 1020 to 1170 fractions/1000 cases.

Without correction for regional cancer burden, demand overestimates of up to 60% would be observed in the south of England, especially London with its younger age structure. Underestimations of up to 20% would be observed in



**Fig 1.** Number of fractions and fractions/million population simulated for each Clinical Commissioning Group in England for the magnetic resonance–linac (MR–linac), based on the clinical indications provided by the MR–linac consortium.



**Fig 2.** Number of fractions and fractions/million population simulated for each Radiotherapy Operational Delivery Network (RODN) in England for the magnetic resonance-linac (MR-linac), based on the clinical indications provided by the MR-linac consortium. Each dot represents a radiotherapy centre with the size corresponding to the number of linacs in the centre [44]. Each RODN has at least one tertiary centre capable of delivering all radiotherapy treatments.

northern England, with a lower population density and a larger proportion of elderly patients. The variations are reduced by focussing on the proportion of cancer cases belonging to an MR-linac indication group and the stage presentation by using fractions/1000 cancer cases. There is still a  $\pm 10\%$  over-/underestimation if a national average is used. The patterns are similar to those observed when using fractions/million, with overestimations typically seen in the south of England and underestimations seen in northern England.

This level of variation shows the need for local-level planning of services utilising local-level data, especially when looking to install a new technology that only targets specific tumour sites. Even when CCGs are grouped into RODNs and an averaging effect might be expected, the variation still occurs. There is still a maximum two-fold difference in the demand across the RODNs in England.

In general, CCG-level stage at presentation data in Malthus are reasonably complete. However, in some disease sites, the quality of available stage at presentation data is not sufficient to provide accurate CCG simulation results. In these cases, high-quality national-level stage at presentation data were used. Overall, cancer data are increasing in quality over time and data that are more granular will be included when made available. This should not affect the results as two-thirds of the total MR-linac fraction burden simulated uses the CCG-level stage presentation data.

The oropharyngeal cancer CDT uses the most assumptions. Local (but comprehensive) data had to be used to determine the proportions of the Malthus stage groupings (I–II, III–IVB and IVC) that were MR-linac eligible, as the target indications were TNM based. Oropharyngeal cancer contributed around 13% to the total MR-linac fraction burden and it has the highest number of fractions/MR-linac patient. It would be recommended that a hospital use its

**Table 4**

Effect on the simulated fraction demand for the magnetic resonance-linac (MR-linac) if hypothetical hypofractionation schemes were applied to stage III lung cancer and intermediate-risk prostate cancer

Cancer site	Standard fractionation regimen			Hypofractionation regimen		
	Average fractions/ MR-linac patient	Total MR-linac fractions	MR-linac fractions as % of all fractions for cancer site	Average fractions/ MR-linac patient	Total MR-linac fractions	MR-linac fractions as % of all fractions for cancer site
Lung	32.3	107 400	36%	15	49 900	21%
Prostate	20	112 100	29%	3	16 800	6%
All cancer sites	–	351 000	16%	–	198 200	11%

own oropharyngeal cancer data to determine the correct proportion of Malthus patients eligible for MR-linac treatment.

This study is designed to aid the implementation of a new technology by calculating the fraction burden and patient numbers to assist with calculations of the number of MR-linacs required in different regions. For the MR-linac, and any new technology, it is non-trivial to translate the number of fractions into throughput until the technology is fully in use with initial teething problems resolved. Any treatment activity measured now will probably be significantly reduced once the equipment is fully optimised for operation in the clinic and staff have been fully trained to use the new technology. Research is underway investigating new MR-guided radiotherapy workflows regarding ‘clinician-lite’ approaches to streamline treatment workflow [45]. Therefore, it may take time before optimal workflows are achieved and these data can be accurately used in modelling.

It would be incorrect to use the throughput of a conventional linac to convert fractions to number of MR-linacs due to the different processes and workflows that will occur. When fully implemented, any MR-guided treatment will probably require more time/fraction. In machine throughput terms this may counterbalance any operational gains made from moderate hypofractionation.

MR-linac patient-specific restrictions, such as the smaller bore size and exclusion of patients with metallic implants, were not included due to the lack of data. Therefore, the results should be treated as initial estimates rather than definitive results.

There is currently uncertainty around what sites would benefit the most from hypofractionated or extreme-hypofractionated regimens and clinical research is being undertaken on this subject. The MR-linac version of Malthus is flexible enough to be adapted to new treatment indications or fractional schemes quickly, to provide updated simulations for service planning.

## Conclusions

Planning the introduction of new treatment technologies across a whole healthcare system is made more complex by regional variations and services should be tailored to the local demographics to ensure adequate access to treatments. Recently, local-level cancer data have become more complete and more readily available, and should be exploited in demand simulations of healthcare services. Here, we have shown the capability of using a discrete-event simulation model, Malthus, to determine the demand for a new treatment technology at a local level. This is especially important in a resource-limited setting, where demand for treatments already outstrips the supply capabilities, during times of economic austerity with calls from governments for cost savings. The simulated variations in demand for the MR-linac should highlight the benefits of combining the local-level data with comprehensive models.

## Data Availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

## Conflicts of Interest

T. Mee reports grants from Elekta MR-linac consortium, grants from Cancer Research UK, grants from Christie Charity, grants from UKRI, during the conduct of the study. K.J. Kirkby reports grants from CRUK ARTNET, grants from Elekta MR-linac Consortium, grants from Christie Charity, during the conduct of the study; grants and non-financial support from Varian, grants from UKRI, grants from CRUK, grants from NIHR BRC, outside the submitted work. R. Jena reports personal fees from Microsoft Research, outside the submitted work. A. Choudhury reports grants from the National Institute of Health Research, Manchester Biomedical Research Centre, grants from Cancer Research, UK, grants from Medical Research Council, UK, grants from Prostate Cancer, UK, grants from Bayer, UK, personal fees from Janssen Pharmaceutical, non-financial support from ASCO, grants and non-financial support from Elekta AB, outside the submitted work. N.F. Kirkby reports grants from CRUK ARTNET, grants from Elekta MR-linac Consortium, grants from Christie Charity, during the conduct of the study; grants from UKRI, grants from CRUK, grants from NIHR BRC, outside the submitted work.

## Acknowledgements

This study was supported by the MR-linac Consortium; the CRUK ART-Net project [grant number C309/A21993]; The Christie Charity; Engineering and Physical Sciences Council [grant number EP/R023220/1]; Science and Technology Facilities Council [grant number ST/N002423/1]; the NIHR blinded Biomedical Research Centre and the NIHR blinded Clinical Research Facility. Elekta AB, Sweden, financially supports the MR-linac Consortium. The funders had no involvement in the study design, analysis or report writing. The authors wish to thank Professor Neil Burnet for his input during the revision of the manuscript. We would also like to thank the reviewers for the useful comments on results presentation for variations in demand, which will be carried forward to future studies.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clon.2021.03.004>.

## References

- [1] Cancer Research UK. Cancer statistics for the UK. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk>. [Accessed 22 March 2021].

- [2] Smittenaar CR, Petersen KA, Stewart K, Moitt N. Cancer incidence and mortality projections in the UK until 2035. *Br J Cancer* 2016;115:1147–1155. <https://doi.org/10.1038/bjc.2016.304>.
- [3] Cancer Research UK. Cancer survival statistics. Available at: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/survival>. [Accessed 7 February 2018].
- [4] Miller KD, Siegel RL, Lin C, Mariotto AB, Kramer JL, Rowland JH, et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin* 2016;66:271–289. <https://doi.org/10.3322/caac.21349>.
- [5] Bentzen SM, Heeren G, Cottier B, Slotman B, Glimelius B, Lievens Y, et al. Towards evidence-based guidelines for radiotherapy infrastructure and staffing needs in Europe: the ESTRO QUARTS project. *Radiother Oncol* 2005;75:355–365. <https://doi.org/10.1016/j.radonc.2004.12.007>.
- [6] Department of Health. Radiotherapy: developing a world class service for England. Available at: [http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/Publications-PolicyAndGuidance/DH\\_074575](http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/Publications-PolicyAndGuidance/DH_074575). [Accessed 2 February 2018].
- [7] Department of Health. Radiotherapy services in England 2012. Available at: <https://www.gov.uk/government/publications/radiotherapy-services-in-england-2012>. [Accessed 10 September 2020].
- [8] Department of Health. Improving outcomes: a strategy for cancer. Fourth Annual Report. Available at: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/388160/fourth\\_annual\\_report.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/388160/fourth_annual_report.pdf). [Accessed 14 September 2020].
- [9] Round CE, Williams MV, Mee T, Kirkby NF, Cooper T, Hoskin P, et al. Radiotherapy demand and activity in England 2006–2020. *Clin Oncol* 2013;25:522–530. <https://doi.org/10.1016/j.clon.2013.05.005>.
- [10] Delaney GP, Barton MB. Evidence-based estimates of the demand for radiotherapy. *Clin Oncol* 2015;27:70–76. <https://doi.org/10.1016/j.clon.2014.10.005>.
- [11] Lievens Y, Dunscombe P, Defourny N, Gasparotto C, Borrás JM, Grau C. HERO (Health Economics in Radiation Oncology): a pan-European project on radiotherapy resources and needs. *Clin Oncol* 2015;27:115–124. <https://doi.org/10.1016/j.clon.2014.10.010>.
- [12] 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 Oncol* 2012;24:1–3. <https://doi.org/10.1016/j.clon.2011.11.009>.
- [13] Round C, Mee T, Kirkby NF, Cooper T, Williams MV, Jena R. The Malthus programme: developing radiotherapy demand models for breast and prostate cancer at the local, regional and national level. *Clin Oncol* 2013;25:538–545. <https://doi.org/10.1016/j.clon.2013.05.006>.
- [14] Jena R, Mee T, Kirkby NF, Williams MV. Quantifying uncertainty in radiotherapy demand at the local and national level using the Malthus model. *Clin Oncol* 2015;27:92–98. <https://doi.org/10.1016/j.clon.2014.11.003>.
- [15] Maughan TS, Illidge TM, Hoskin P, McKenna WG, Brunner TB, Stratford IJ, et al. Radiotherapy research priorities for the UK. *Clin Oncol* 2010;22:707–709. <https://doi.org/10.1016/j.clon.2010.03.006>.
- [16] Mackay RI, Burnet NG, Green S, Illidge TM, Staffurth JN. on behalf of the NCRI CTRAD Executive Group. Radiotherapy physics research in the UK: challenges and proposed solutions. *Br J Radiol* 2012;85:1354–1362. <https://doi.org/10.1259/bjr/61530686>.
- [17] Yan D, Lockman D, Martinez A, Wong J, Brabbins D, Vicini F, et al. Computed tomography guided management of inter-fractional patient variation. *Semin Radiat Oncol* 2005;15:168–179. <https://doi.org/10.1016/j.semradonc.2005.01.007>.
- [18] Chin S, Eccles CL, McWilliam A, Chuter R, Walker E, Whitehurst P, et al. Magnetic resonance-guided radiation therapy: a review. *J Med Imaging Radiat Oncol* 2020;64:163–177. <https://doi.org/10.1111/1754-9485.12968>.
- [19] Mutic S, Dempsey JF. The ViewRay System: magnetic resonance-guided and controlled radiotherapy. *Semin Radiat Oncol* 2014;24:196–199. <https://doi.org/10.1016/j.semradonc.2014.02.008>.
- [20] Keall PJ, Barton M, Crozier S. on Behalf of the Australian MRI-Linac Program. The Australian magnetic resonance imaging—linac program. *Semin Radiat Oncol* 2014;24:203–206. <https://doi.org/10.1016/j.semradonc.2014.02.015>.
- [21] University of Alberta. Linac-MR. Available at: <http://www.mp.med.ualberta.ca/linac-mr/>. [Accessed 8 February 2021].
- [22] Lagendijk J, Raaymakers BW, van Vulpen M. The magnetic resonance imaging—linac system. *Semin Radiat Oncol* 2014;24:207–209. <https://doi.org/10.1016/j.semradonc.2014.02.009>.
- [23] Health Care Business. PPI to purchase Elekta MR-linac systems for £25 million. Available at: <https://www.dotmed.com/news/story/42728>. [Accessed 16 July 2020].
- [24] Van Dyk J, Zubizarreta E, Lievens Y. Cost evaluation to optimise radiation therapy implementation in different income settings: a time-driven activity-based analysis. *Radiother Oncol* 2017;125:178–185. <https://doi.org/10.1016/j.radonc.2017.08.021>.
- [25] Care Quality Commission. Delivering cost effective care in the NHS. Available at: [https://www.cqc.org.uk/sites/default/files/20151028\\_delivering\\_cost\\_effective\\_care\\_in\\_the\\_NHS.pdf](https://www.cqc.org.uk/sites/default/files/20151028_delivering_cost_effective_care_in_the_NHS.pdf). [Accessed 8 February 2018].
- [26] Aggarwal A, Sullivan R. Affordability of cancer care in the United Kingdom — is it time to introduce user charges? *J Cancer Policy* 2014;2:31–39. <https://doi.org/10.1016/j.jcpc.2013.11.001>.
- [27] Tree AC, Huddart R, Choudhury A. Magnetic resonance-guided radiotherapy — can we justify more expensive technology? *Clin Oncol* 2018;30:677–679. <https://doi.org/10.1016/j.clon.2018.08.013>.
- [28] Goldwein J. MR Linac consortium clinical indications. Personal communication to Mee T. 20/12/2016.
- [29] Corradini S, Alongi F, Andratschke N, Belka C, Boldrini L, Cellini F, et al. MR-guidance in clinical reality: current treatment challenges and future perspectives. *Radiat Oncol* 2019;14:92. <https://doi.org/10.1186/s13014-019-1308-y>.
- [30] Kerkmeijer LGW, Fuller CD, Verkooijen HM, Verheij M, Choudhury A, Harrington KJ, et al. The MRI-Linear Accelerator Consortium: evidence-based clinical introduction of an innovation in radiation oncology connecting researchers, methodology, data collection, quality assurance, and technical development. *Front Oncol* 2016;6:215. <https://doi.org/10.3389/fonc.2016.00215>.
- [31] Symonds P. *Walter & Miller's textbook of radiotherapy: radiation physics, therapy and oncology*, 7th ed. London: Churchill Livingstone; 2012.
- [32] Malthus. CDTs 2019 updates. Available at: <http://www.camradiotherapy.org.uk/malthus>. [Accessed 16 July 2020].
- [33] Roach MC, Bradley JD, Robinson CG. Optimizing radiation dose and fractionation for the definitive treatment of locally advanced non-small cell lung cancer. *J Thorac Dis* 2018;10:S2465–S2473.

- [34] Murray J, Tree AC. Prostate cancer – advantages and disadvantages of MR-guided RT. *Clin Transl Radiat Oncol* 2019;18: 68–73. <https://doi.org/10.1016/j.ctro.2019.03.006>.
- [35] Mee T. *Monte Carlo applications for local treatment healthcare usage simulations*. PhD Thesis. University of Surrey; 2015.
- [36] The Royal College of Radiologists. *Radiotherapy dose fractionation*, 3rd ed. 2020. Available at: [https://www.rcr.ac.uk/system/files/publication/field\\_publication\\_files/brfo193\\_radiotherapy\\_dose\\_fractionation\\_third-edition.pdf](https://www.rcr.ac.uk/system/files/publication/field_publication_files/brfo193_radiotherapy_dose_fractionation_third-edition.pdf). [Accessed 29 June 2020].
- [37] Sanderson B, McWilliam A, Faivre-Finn C, Kirkby N, Jena R, Mee T, et al. Using the Malthus programme to predict the recruitment of patients to MR-linac research trials in prostate and lung cancer. *Radiother Oncol* 2017;122:159–162. <https://doi.org/10.1016/j.radonc.2016.11.014>.
- [38] Office for National Statistics. Subnational population projections for England. Available at: <https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationprojections/bulletins/subnationalpopulationprojectionsforengland/previousReleases>. [Accessed 2 February 2018].
- [39] NCRAS. Survival by stage. Available at: [http://www.ncin.org.uk/publications/survival\\_by\\_stage](http://www.ncin.org.uk/publications/survival_by_stage). [Accessed 10 January 2018].
- [40] Barclay ME, Lyrtzopoulos G, Greenberg DC, Abel GA. Missing data and chance variation in public reporting of cancer stage at diagnosis: cross-sectional analysis of population-based data in England. *Cancer Epidemiol* 2018;52:28–42. <https://doi.org/10.1016/j.canep.2017.11.005>.
- [41] Operational NHS. delivery networks for adult external beam radiotherapy services. Available at: <https://www.england.nhs.uk/wp-content/uploads/2019/01/Operational-Delivery-Networks-for-External-Beam-Radiotherapy-Services-adults.pdf>. [Accessed 21 November 2019].
- [42] MISO. *CCG Mapping Copyright © 2013, Re-used with the permission of the Health and Social Care Information Centre 2017. All rights reserved.*
- [43] Tableau Software. *Tableau Desktop Professional Edition 2018. 2. 0 2019.*
- [44] IAEA. Directory of radiotherapy centres. Available at: <https://dirac.iaea.org/>. [Accessed 12 June 2019].
- [45] Hales RB, Rodgers J, Whiteside L, McDaid L, Berresford J, Budgell G, et al. Therapeutic radiographers at the helm: moving towards radiographer-led MR-guided radiotherapy. *J Med Imaging Radiat Sci* 2020;51:364–372. <https://doi.org/10.1016/j.jmir.2020.05.001>.