Title page

Title: Stereotactic ablative body radiotherapy in patients with oligometastatic cancers: a national prospective, single-arm, evaluation study.

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Word count: 3962
Keywords: SABR, SBRT, oligometastasis, overall survival, adverse events, registry

Summary

Background

Stereotactic ablative body radiotherapy (SABR) is increasingly being used to treat oligometastatic cancers, but with the exception of a recent phase II randomized controlled trial (RCT) there is currently no high level evidence on which to base policy making. It is therefore important to provide additional evidence from a real-world setting. Here, we present the results of a national prospective, single-arm, observational, evaluation study of patients with extracranial oligometastases undergoing SABR, which provides the largest data set, to our knowledge, on outcomes for this population thus far.

Methods

In 2015, NHS England launched a Commissioning through Evaluation (CtE) scheme that funded the creation and analysis of a prospective national evaluation study of patients with solid cancer and extracranial oligometastates treated with SABR. This study was conducted at 17 NHS centres in England. Patients aged 18 years or older with a disease-free interval of greater than six months (with the exception of synchronous colorectal liver metastases) and one to three metastatic lesions, World Health Organization performance status of ≤2, and a life expectancy of at least 6 months were eligible for the scheme. Overall survival, local control, adverse events and quality of life were analysed.

Findings

Between 2015 and 2019, 1422 patients were recruited from 17 hospitals in England. The median age of patients was 69 years (IQR: 62 to 76 years), and 66.6% were men. The commonest primary tumours were prostate (28.6%), colorectal (27.9%) and renal cancer (10.1%). Median follow-up for the cohort was 13 months. Overall survival was 92.3% (95% CI: 90.5-93.9%) at one year and 79.2% at two years (95% CI: 76.0-82.1%). The local control rate was 86.9% (95% CI: 84.6-88.9%) at one year and 72.3% (95% CI: 68.7-75.6%) at two years. Adverse event rates were low with grade 3 toxicity rates of 4.4% (95% CI: 3.3 - 5.4%) and grade 4 toxicity rates of 0.6% (95% CI: 0.2 - 1.0%). Quality of life did not change significantly from baseline to final follow-up.

Interpretation

In our large national evaluation study of patients with extracranial oligometastatic cancer, the use of SABR is associated with high overall survival and local control rates, as well as low toxicity. These findings will need to be confirmed by an adequately powered phase III RCT.

Funding

National Institute for Health and Care Excellence, NHS England

Research in context

Evidence before this study

SABR for patients with extracranial oligometastatic cancer was not routinely commissioned by the National Health Service (NHS) in England. NHS guidance states that SABR should only be provided to patients with extracranial oligometastatic cancer in the context of clinical trials to ensure that the evidence base for this treatment continues to accrue.

We searched the Medline, Embase, Cochrane Database of Systematic Reviews (CDSR) and Cochrane Controlled Register of Trials (CENTRAL) for studies of patients with extracranial oligometastatic cancer treated with SABR. The search was restricted to studies published from January 2009 to March 2019) and included studies analysing patients with metachronous, extracranial metastases (up to three metastases). The search strategy used terms related to "oligometastatic" (e.g. oligomet* or oligo-met* or oligo met*) and to SABR (e.g. SABR or stereotactic ablati* or stereotactic body radio* or stereotactic radio*). The reference lists of all relevant retrieved studies were also searched. The included studies were critically appraised and their quality was assessed using the National Service Framework for Long-Term Conditions evidence assessment framework (1). The search revealed 17 relevant studies consisting of two small phase II RCTs (2, 3) and a number of mostly retrospective single-arm cohort studies and an absence of phase III RCTs.

Added value of this study

This prospective study found that the use of SABR in patients with metachronous oligometastatic cancer achieved a 92.3% and 79.2% overall survival rate at one and two years, respectively, as well as low rates of severe adverse events. These study findings are consistent with the phase II RCT evidence with regards to overall survival and represent the strongest real-world evidence to support the use of SABR in this patient cohort.

Implications of all the available evidence

This evaluation study strengthens the available evidence in the literature supporting the use of SABR in appropriately selected patients with metachronous extracranial oligometastases and resulted in routine commissioning of SABR for treating patients with oligometastatic disease by NHS England in 2019 (4).

Introduction

Metastatic cancer is diagnosed in approximately 140,000 patients in England per year (5). The conventional treatment of patients with metastatic, solid tumours is with palliative intent, using chemotherapy and other systemic treatments, with the intent of delaying disease progression, improving quality of life and possibly extending life. Sometimes metastatic disease is diagnosed when only a limited number of metastases can be detected. This 'oligometastatic' state is a proposed entity between localised and widely disseminated cancer. These patients appear to have a better prognosis than most patients with metastatic disease and aggressive metastasis-directed therapy may modify disease outcomes (6).

SABR uses external beam radiation therapy to deliver a high, biologically-effective dose (BED) to the tumour while minimising the dose received by the surrounding normal tissues. It could thus minimise radiotherapy treatment toxicity and side effects (7). Common components include high doses per fraction, small number of fractions and the requirement of specialised planning, treatment delivery and quality assurance (8).

In the last decade, evidence from multiple non-comparative retrospective studies suggests that patients with a limited number of metastases treated with SABR achieve high local control (LC) rates with minimal toxicity (9). Early findings also suggest SABR may delay the need for systemic therapy and improve progression-free survival (2, 10, 11). A recently published phase II RCT by Palma et al (2019) provided the first prospectively collected comparative data that SABR leads to improved survival in comparison with the standard of care at the expense, however, of treatment-related toxicity and deaths (3).

A common criticism of RCTs is that they often include patients not representative of real-world clinical practice. In addition, SABR delivery requires specialist equipment and training, and its clinical effectiveness and safety depends on successful implementation in everyday clinical practice. Further data is, therefore, required to determine whether the survival benefit demonstrated by Palma et al. (2019) can be reproduced in real world practice and to investigate the incidence of adverse events in this setting.

In 2015, NHS England launched the Commissioning through Evaluation (CtE) scheme for SABR. The scheme, which is part of NHS England's Evaluative Commissioning Programme, provided funding for patients with extracranial oligometastatic cancer to access SABR within the NHS (12). Patients treated under the scheme participated in a prospective registry-based

clinical effectiveness and safety evaluation study. This report summarises the findings of the scheme.

Methods

Study design

This prospective, single-arm, observational, evaluation study was carried out between June 2015 and January 2019 in 17 commissioned NHS radiotherapy centres in England (supplementary data). All data captured as part of the study were uploaded to a national radiotherapy registry (PROPEL) developed for the purpose of the study and managed by University Hospitals Birmingham (UHB). Planning and oversight of the study was provided by a multidisciplinary steering group, which included clinical and academic experts, patient representatives, and NHS England commissioners. It was estimated that approximately 500 patients per year would be eligible to receive SABR to give a total of 1500 over three years. Appropriate regulatory approvals, including ethical approval, were obtained in all participating centres (REC reference: 16_NE_0285). All patients provided written informed consent.

Patient selection

Patients with a radically treated and controlled histologically-confirmed primary carcinoma (excluding haematological malignancies) and three or fewer sites of metachronous extracranial metastases (with the exception of synchronous colorectal liver metastases), amenable to treatment with SABR but unsuitable for surgery, were considered for inclusion. In order to identify patients with oligometastases, PET-CT or whole body diffusion-weighted MRI, where undertaken as appropriate and available. Brain imaging to exclude occult brain metastases was used prior to SABR in cancers with a high propensity for cerebral metastases. Metachronous disease was specified as the development of metastases more than six months after a primary cancer is treated. A maximum size of six cm for any single metastasis (five cm for metastases located in the lung or liver), a life expectancy of > six months and a World Health Organization (WHO) performance status (PS) ≤ two was also required. All patients' eligibility was assessed in a multi-disciplinary oncology meeting. Further details on patient eligibility criteria can be found in the supplementary data.

Treatment and follow-up

Treatment dose and fractionation schedules were based on the UK SABR Consortium guidelines (13) and were dependant on metastasis size and location (14). Prescribed doses ranged from 24-60 Gy administered in three to eight fractions (see supplementary data). With the exception of hormone therapy, administration of systemic treatment had to be discontinued for four (chemotherapy) and two weeks (targeted agents) prior to SABR. Each participating site was required to participate in an accreditation programme led by the national Radiotherapy Trials Quality Assurance team prior to treating patients (15). This accreditation programme included test cases with clinician contouring and radiotherapy planning detail assessment. Each site had to submit their first treatment plans for peer review. Patients were followed-up in the oncology clinic every three months post-treatment for a maximum of two years. Patients could receive further radiotherapy or systemic treatments for relapse after SABR completion at the discretion of the treating clinician.

Outcomes

Overall survival (OS) was the primary outcome and it was defined as the duration from SABR treatment until death from any cause. An estimated OS target rate of 70% and 50% for 1-and 2-years, respectively, was set based on reported from a systematic review we conducted in 2015. Where patients were still alive at the final documented clinical visit, they were censored at that date in the analysis. Median survival time was defined as the amount of time at which half of the patients are still alive. This cannot be estimated when more than 50% of all patients are alive at the point of analysis. Local control was defined as no change or reduction in the size of the lesion treated and was assessed by the local reporting radiologist and treating clinicians. New metastasis free survival was analysed as a post hoc endpoint. Time to local or distant progression was defined as the duration from SABR treatment to the earliest detection of tumour progression or new metastases assessed by medical imaging. Patients with no progressive disease recorded were censored at the last follow-up. Adverse events were assessed and recorded at each three month follow-up visit by an experienced member of the oncology team using the Common Terminology Criteria for Adverse Events version 4.0 criteria (16). The EuroQOL-5D-3L (EQ-5D-3L) questionnaire was used to collect quality of life data at baseline and at each follow-up appointment.

Data linkage

Mortality data from the Office for National Statistics (ONS) covering the years 2015-2019 for patients included in the scheme were requested by NHS Digital. These patient records were linked with patient-level data captured in the PROPEL database to enable accurate mortality data to be captured. The PROPEL and ONS database were linked in January 2019.

Statistical analysis

Patient and treatment characteristics are presented as descriptive statistics. The number of patients eligible for treatment was estimated based on a review of the literature and projected one and two year OS. Median follow-up time with inter-quartile ranges (IQR) were calculated where appropriate. Statistical analyses were focused on overall patient survival time, toxicity and LC.

Survival function estimates with 95% confidence intervals were calculated for one- and two-years from the start of SABR treatment using the Kaplan-Meier method. Where there were fewer than 5 deaths in a group or subgroup of patients, Kaplan-Meier estimates were not calculated as they are considered unreliable (17). Categorical covariates such as gender, age, tumour histology, site of first metastasis, number of metastases, region of first metastasis and WHO PS were included in univariate Cox regressions followed by multivariable analysis to evaluate their possible influence on clinical outcomes.

The multivariable regression models were constructed as follows: Firstly, all candidate predictors were grouped into clusters representing: patient characteristics (sex, age, WHO PS), cancer characteristics (primary tumour site, site of first metastasis, number of metastases, region of metastasis) and treatment characteristics (biologically effective dose, post-SABR systemic treatment). Univariate analyses were conducted by means of log rank tests with an assumed type-I error of 0.10. Cox proportional hazards regression model were applied for candidate variables with p-values ≤0.10, initially, separately for each cluster and then combined. All the analyses were conducted on the total sample (n=1,422 patients) and repeated for the subsample of patients with a follow-up longer than 18 months (n=700).

All descriptive statistics and time to event analyses were conducted in STATA version 15.1 and STATA graph addition (18). SPSS version 25 was used to aggregate and transform the data.

Role of funding source

One of the funders (NICE) of the study had a role in the study design, and data collection, data analysis and writing of this report.

Results

Patient and treatment characteristics

Between June 2015 and January 2019, the study collected outcomes from 1422 patients with oligometastatic cancer. Patient screening data was not collected. Study completion originally planned for May 2018, was extended by 6 months due to the consecutive roll-out of the study and the low recruitment rate during the first year. Data from 1113 patients were linked to the ONS registry to cross-check deaths with those reported in the study. The median age of patients was 69 years (IQR 62-76 years), and 947 (66.6%) were male. The most common primary tumours were prostate (406 patients, 28.6%), colorectal (397 patients, 27.9%) and renal cancer (143 patients, 10.1%). 1074 patients were treated for a solitary metastasis (75.1%). The most commonly treated sites were lymph nodes (31.3%) and the lung (29.3%). Over 95% had a WHO performance score of 0 or 1 (95.4%) and 60.0% had received prior systemic treatment either in the adjuvant or metastatic setting. PET_CT was not mandated for staging, however 62% of patients underwent PET-CT before enrolment. Baseline patient and treatment characteristics are shown in Table 1.

Survival

Median follow-up time was 13 months (IQR 6 – 23 months). Overall survival estimates at one- and two-years were calculated along with a corresponding Kaplan-Meier plot (Figure 1), the median OS time was longer than 24 months. Overall survival was 92.3% (95% CI: 90.5 - 93.9%) at one year and 79.2% (95% CI: 76.0 - 82.1%) at two years. There was variation across the primary tumour sites, with the two-year OS ranging from 38.0% for patients with melanoma to 94.6% for patients with prostate cancer (Table 2a). For patients with a follow-up of longer than 18-months, OS was not significantly different compared to OS for the entire cohort.

Local control

Overall LC estimates at one- and two-years were calculated along with a corresponding Kaplan-Meier plot (Figure 2), median time to LC failure was longer than 24 months. Local

control was 86.9% (95% CI: 84.6 - 88.9%) at one year and 72.3% (95% CI: 68.7 - 75.6%) at two years.

Metastasis free survival

New metastasis free survival (MFS) estimates at one- and two-years were calculated along with a corresponding Kaplan-Meier plot, the median time was 24 months. Overall MFS was 84.0% (95% CI: 81.4 - 86.3%) at one year and 52.0% (95% CI: 47.4 - 56.4%) at two years (see supplementary data).

Toxicity

A summary of the percentages of patients with 1 or more adverse event reported is shown in Table 3. 959 patients experienced a total of 4795 adverse events, of which 70 (5%) were grade three or above (supplementary data). Grade three toxicity rates of 4.4% (95% CI: 3.3 - 5.4%) and grade 4 toxicity rates of 0.6% (95% CI: 0.2 - 1.0%) were recorded. The most common events were mild fatigue and mild cough. No grade 5 toxicity was reported.

Quality of life

Overall, quality of life outcomes (EQ5D) were minimally different from baseline to final follow-up. There was no significant change over time even in the first 3 months after treatment. This correlates well with the low adverse events rates observed and is an indication that patients tolerated SABR well as they normally find radiotherapy courses a challenge (supplementary data).

Multivariable analyses

After adjusting for age and gender OS was affected by primary tumour histology. Patients with PS=2 had double the Hazard Ratio (HR) compared to people with PS=0 (HR: 1.78; 95%CI: 1.01-3.17). Compared to lung cancer, HRs were smaller for patients with breast (HR: 0.38; 95%CI: 0.15-0.93); prostate (HR: 0.14; 95%CI: 0.06-0.34); renal (HR: 0.36; 95%CI: 0.16-0.77); and colonic cancer (HR: 0.51; 95%CI: 0.27-0.95).

Local control was influenced by primary tumour histology, number of metastases and WHO PS. Using lung cancer as a reference category, LC was less likely for patients with colon cancer (HR: 2.70, 95%CI:1.14-6.41), melanoma (HR: 4.07; 95%CI:1.49-11.17) and rectal cancer (HR: 2.84, 95%CI:1.18-6.85). Patients with one metastasis had lower HR compared to those with >1 metastases (HR: 1.50, 95%CI: 1.09-2.08). Finally, age (HR: 1.00; 95%CI: 1.00-1.01), and primary

tumour histology influenced the rate of adverse events. (See supplementary data for full details.)

Discussion

This study is the largest prospective, registry-based analysis to examine the effectiveness and safety of SABR in patients with oligometastatic cancer. These results show that contemporary patients with metachronous extracranial oligometastases treated with SABR in a real-world setting achieve high rates of one- and two-year OS with low rates of severe toxicity. To our knowledge, the findings here represent the strongest non-randomised real-world evidence characterising the use of SABR in this patient cohort. This study compliments the findings of Palma et al. (2019) with regard to OS but indicates a lower toxicity rate in our cohort.

Other single-arm, retrospective registries have provided evidence on the clinical effectiveness of SABR in patients with oligometastatic cancer (19-22). They reported one- and two-year OS rates ranging from 70-74% and 47-60%, respectively, with both outcomes lower than our study findings, however our cohort has a very short follow-up and only two thirds of patients had visceral metastases. The earliest of these studies report treatment from 1997 where the population, intervention and other aspects of study design may be less comparable to a contemporary cohort. These studies often treated patients with lower radiotherapy doses and included patients with site-specific metastases such as only liver or lung which were less well represented in our patient cohort.

Studies with similar population and intervention characteristics support our OS findings. Sutera et al. (2019), a study with a median follow-up of 42 months, reported a one- and two-year OS rate of 84 and 63%, respectively. Similarly, Palma et al. (2019) reported OS rates of 86% and 70% with SABR and 86% and 60% with standard care, which was comprised of palliative radiotherapy or chemotherapy. Both studies recruited patients with oligometastases from different primary cancers with various lesion locations.

Palma et al. (2019) concluded that further research should aim to provide evidence of the OS benefits for tumour-specific groups in formal phase III trials. It is worth noting that 41% of patients recruited in the Palma study had breast (20%) or prostate (21%) cancer in the SABR arm compared to 15% of patients with breast and 6% with prostate in the standard care arm. Patients with low burden metastatic prostate cancer have a better prognosis than those with

other types of metastatic cancer (23, 24) and there is additional evidence that one and two-year survival rates in patients with prostate oligometastatic cancer is close to 100% (2, 25). Therefore the comparator arm of the trial may be biased towards poorer outcomes. Although a post-hoc sensitivity analysis of SABR-COMET excluding patients with prostate cancer was consistent with a treatment benefit with 5-year OS rates of 16.2% (95% CI: 5-32%) vs. 33.1% (95% CI: 20-47%) respectively, failed to achieve statistical significance (p=0.085) (26). Indeed, the highest one- and two-year OS rates reported in the literature are from a study including only patients with prostate cancer and bone/nodal metastases, all considered as good prognostic factors (25). The tumour-specific analysis of patients in our cohort showed great variability in OS, with two-year OS ranging from 38.0% for patients with melanoma to 94.6% for patients with prostate cancer.

Although the oligometastatic state has been described as that where metastases are limited in number and extent, a precise and accepted definition is lacking (27). Some studies included patients with up to 5 metastases (19, 20, 28, 29) while this study allowed up to three. In Palma et al. (2019) 17% of patients had four or five metastases. As such, the results of Palma et al. (2019) may be most relevant to patients with one to three oligometastases. In our analysis the number of metastases had no impact on OS. Although the impact of the number of oligometastases on survival is unknown, a higher number of metastases increases the likelihood that the disease is systemic rather than oligometastatic (9). A recent consensus recommendation by the European Society for Medical Oncology and the European Organisation for Research and Treatment of Cancer included the number of metastases as a quantitative characteristic of oligometastatic cancer but did not provide a definitive cut-off (30). Instead, it proposed a distinction between genuine oligometastatic cancer, defined as the absence of polymetastatic disease in the patient's history indicating that indicates a cancer with low metastatic capacity and induced oligometastatic cancer following systemic treatment. Two ongoing RCTs (31, 32) recruiting patients with 1-3 and 4-10 metastases, respectively may provide more evidence on the effect of the number of metastases on survival in patients with oligometastatic cancer.

Our adverse events rates were lower than the Palma et al. (2019) study but in agreement with other published studies (25, 29, 33-36) (19, 21, 22) including other phase II RCTs (10, 11) investigating the role of SABR as consolidative treatment in oligometastatic disease. With the exception of the Palma et al. (2019) RCT, the literature consistently reports an absence of grade

4 and 5 toxicity and low rates of grade 3 or less adverse events. Our study had a relatively high number of treated lymph nodes (31.3%), explained by the use of PET for staging, and 56% of the cohort comprised of prostate and colorectal cancers. These might have incurred less events as the volume of disease is smaller than visceral disease, and dose prescribed is lower. This is, however, not a unique feature of our study. Indeed, a number of other studies (10, 25, 29, 36) with high rates of treated lymph nodes (ranging from 16.5% to 61%) have reported similarly lower adverse events as our study and they are in odds with the results of SABR-COMET. Specifically, the study by Gomez et al. (2016) was also a phase II RCT in which SABR was given as part of local consolidative therapy and more than 50% of the included patients had advanced nodal disease. Gomez et al. (2016) did not report any grade 4 adverse events or deaths due to treatment, consistent with our findings and at odds with SABR-COMET. In addition, of the three treatment related deaths in the Palma et al. (2019) study, one was a result of radiation pneumonitis, one pulmonary abscess and third due to subdural haemorrhage following gastric ulcer, respectively. These may all be related to treating tumours centrally located in lung with high doses. This was avoided in our study.

This study included various types of primary cancer and it was therefore not possible to outline the standard of care systemic therapy. Compared with most systemic treatments delivered over a period of 6 months to patients with metastatic disease, SABR is a non-invasive outpatient treatment that has minimal toxicity and excellent local control with high acceptability in terms of convenience and societal costs. The exact number of further cycles of systemic therapy, and the drugs used, could not be reliably ascertained for all patients as they were often treated at other oncology centres during the follow-up period. Receipt of additional systemic treatment did not have an impact on outcomes in multivariable analyses, a similar finding to other studies (3, 29).

This study has several strengths. Firstly, the scheme prospectively recruited and analysed the largest contemporary cohort of patients with metachronous extracranial oligometastatic cancer. All centres taking part in the scheme had to undergo a nationally-assured training system for SABR treatment, not only ensuring consistency of the intervention across a multicentre setting but also potentially increasing safety. In addition, patients in the registry were linked to ONS data, which provided a method to triangulate the mortality event rates, reducing uncertainty.

The authors do acknowledge several limitations of the study. The consecutive roll-out of the study and the relatively low recruitment rate during the first year resulted in a relatively short follow-up period. As a result, median OS was not reached and it is not possible to evaluate the long-term safety and efficacy of SABR. We tried to mitigate this issue by performing sensitivity analysis on the subsample of patients with a follow-up longer than 18 months, this confirmed the full analysis's findings. This study included patients with multiple primary cancer types. Outcomes such as OS are influenced by the tumour's primary histology. Histological diagnosis is known to affect prognosis and can be expected to affect sensitivity to SABR. The number and effectiveness of systemic therapy options also varies greatly between tumour types, as does the sensitivity of staging investigations. In terms of imaging investigations, PET-CT was recommended but not mandated, as the indication for PET-CT varies across the cancer spectrum. Approximately 60% of our patients were staged using PET-CT which is higher than the 45% and 52% reported in Palma et al. (2019) and Gomez et al. (2016) respectively. All these factors can be expected to affect outcome following SABR and are likely to explain the differences we observed in one- and two-year survival rates between primary tumour cohorts. These factors were also the reason why this study did not report progression-free survival, a commonly used surrogate outcome. Our study adopted a pragmatic approach to adverse event reporting that may have missed treatment related toxicity because of a potential lack of site monitoring. The Kaplan-Meier analysis assumed that there was "no event" unless an event was recorded. As a result, events cannot account for patients lost to follow-up such as due to disease progression and this can potentially lead to detection bias. For the OS analysis, this limitation is mitigated using the ONS database for data triangulation. For LC, the study adopted a reporting method that was based on the absence or presence of any progression without using objective size measurements. This limits the generalisability of the results and introduces potential detection bias.

The primary aim of the study was to assess the clinical effectiveness and safety of SABR in a real-world population, specifically to inform national policy making. This imposed additional time and resource constraints that are not always imposed on RCTs. Two-year follow up was selected pragmatically to allow meaningful estimates of clinically relevant outcomes (1- and 2-year overall survival) whilst aligning with the timeline requirements of policy making. It will be important for national data collections such as this to take advantage of research opportunities related to a national cohort (often not possible for RCTs). There would be information

governance requirements, but long term outcomes could be assessed using data linkage to routine information. Prior to our treatment scheme, SABR for oligometastases was not funded by the NHS in England. Our scheme facilitated the introduction of a new technologically advanced radiotherapy techniques in a short period of time and on a national basis whilst providing excellent clinical outcomes and low rates of treatment related toxicity. This model of working with common treatment protocols and centralised quality assurance could be employed to roll out SABR and other innovative radiotherapy techniques to other radiotherapy centres in the United Kingdom or worldwide.

This study confirms excellent early safety and efficacy data for a large national cohort of patients with extracranial metachronous oligometastatic cancer treated with SABR. The evidence provided contributes to a growing foundation of observational and randomised studies of SABR in this population.

Acknowledgments

The authors thank the patients who took part in the study and the clinical teams across the 17 NHS Trusts involved in the scheme for their work in recruiting and treating patients, and collecting patient data. The authors would also like to acknowledge the team running the PROPEL database and especially Libby Zou and Sandy Sahdra for providing database management support for this project. We would also like to thank Dr Antony Carver for his insights over BED calculation and a/b ratio selection. MAH declare funding from the NIHR Biomedical Research Centre at University College London Hospitals National Health Service Foundation Trust, outside the submitted work.

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Tables

Table 1: Baseline clinical and procedural characteristics

Characteristic	N	%
Number of patients	1,422	100%
Age group (years)		
19-29	31	2.2%
30-39	20	1.4%
40-49	52	3.6%
50-59	174	12.2%
60-69	436	30.7%
70-79	501	35.2%
80+	208	14.6%
Age (years) – Median (IQR)	69	(62 to 76)
Sex		
Male	947	66.6%
Female	475	33.4%
WHO performance status		
0	1000	71.1%
1	342	24.3%
2	64	4.6%
Total WHO performance status	1406	
Missing WHO performance status	16	1.1%
Primary tumour diagnosis		
Prostate cancer	406	28.6%
Colorectal cancer	397	27.9%
Renal cancer	143	10.1%
Breast cancer	78	5.5%
Lung cancer	64	4.5%
Melanoma	58	4.1%
Other	276	19.4%
Site of treated metastases		
Lung	411	29.3%
Spine	132	9.4%
Bone	169	12.1%
Adrenal	41	2.9%
Liver	135	9.6%
Lymph nodes	439	31.3%
Other	74	5.3%
Missing Site of first metastases	21	1.5%
Number of metastases		
1	1074	75.5%
2	279	19.6%
3	68	4.8%
Missing Number of metastases	1	0.1%
Prior systemic therapy		
Yes	850	59.8%

No	572	40.2%
Types of prior systemic therapy		
Chemotherapy	455	53.5%
Hormonal treatment	263	27.7%
Other	132	15.5%
Post-SABR systemic therapy		
Chemotherapy	134	38%
Hormonal treatment	44	13%
Immunotherapy	121	35%
Targeted therapy	5	1%
Other	45	13%
Number of fractions		
3	792	55.7%
5	468	32.9%
8	148	10.4%
Other	8	0.6%
Missing	6	0.4%
Biologically effective dose* - Gy		
Median (IQR)	105 (72-130)	NA
*Calculated using an a/b ratio of 3 for breast and prostate cancer and 10 for all other primary cancer types.		

Table 2a: Overall survival estimates by primary tumour histology

Primary Site	Number of patients	Survival interval	Survival probability	95% Confidence interval
Prostate cancer	406	1 Year	Not calculable*	
		2 Year	94.6%	90.4 to 97.0%
Colonic cancer	233	1 Year	92.0%	86.6 to 95.3%
		2 Year	80.3%	71.8 to 86.5%
Rectal cancer	164	1 Year	93.7%	87.2 to 97.0%
		2 Year	77.8%	66.5 to 85.7%
Renal cancer	143	1 Year	95.3%	89.0 to 98.0%
		2 Year	82.4%	70.6 to 89.8%
Lung cancer	64	1 Year	80.2%	67.1 to 88.6%
		2 Year	65.4%	50.6 to 76.7%
Melanoma	58	1 Year	Not calculable*	
		2 Year	60.5%	38.0 to 77.0%
*Note that survival estimates are only provided when there are more than 5 events (deaths).				

Table 3: Summary table for adverse events: percentage of patients with 1 or more adverse event reported

CTCAE grade	Number of patients with adverse events	Percentage of patients with adverse events	95% confidence interval
All grades (any adverse event)	959/1422	67.4%	65.0 - 70.0%
Grade 3	62/1422	4.4%	3.3 – 5.4%
Grade 4	8/1422	0.6%	0.2 - 1.0%
CTCAE = Common Terminology Criteria for Adverse Events			

Figures

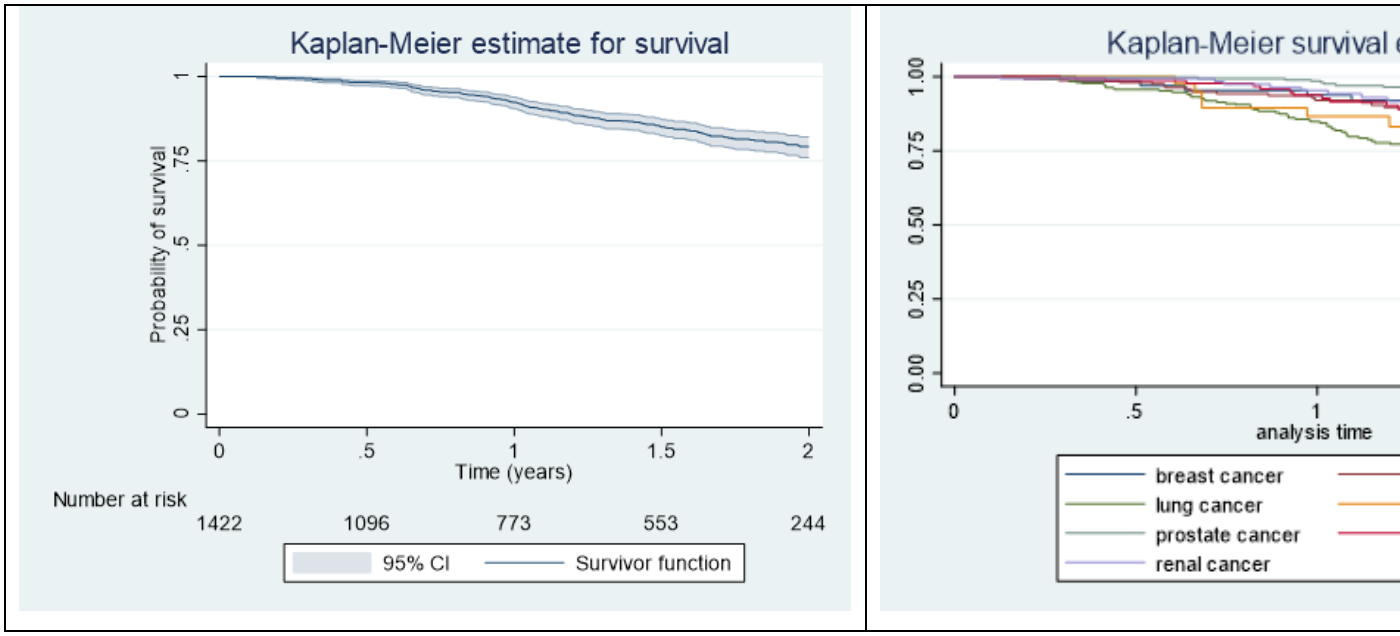

Figure 1: Kaplan-Meier estimate for overall survival for the whole cohort and per primary cancer.

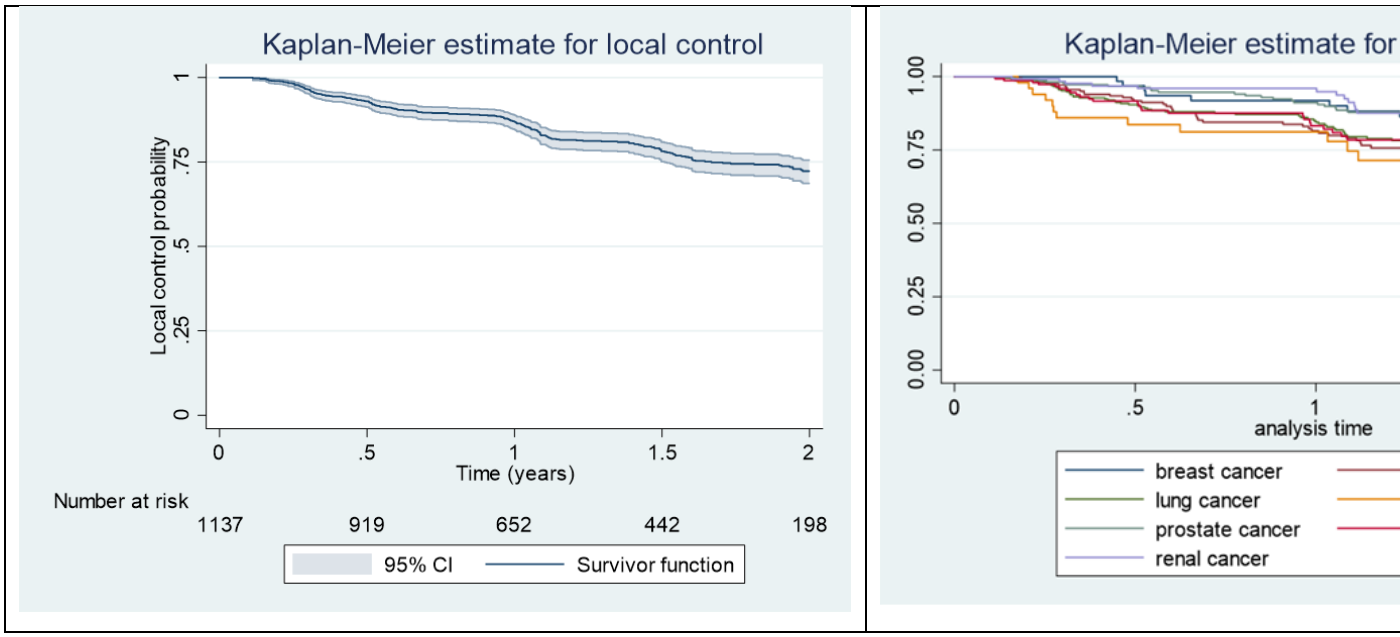

Figure 2: Kaplan-Meier estimate for local control for the whole cohort and per primary cancer.