Metastatic spine tumor epidemiology: comparison of trends in surgery across two decades and three continents.

Authors

Ernest Wright[a], Federico Ricciardi[b], Mark Arts[c], Jacob M. Buchowski[d], Chun Kee Chung[e], Maarten Coppes[f], Alan Crockard[a], Bart Depreitere[g], Michael Fehlings[h], Norio Kawahara[i], Chong Suh Lee[j], Yee Leung[k], Antonio Martin-Benlloch[l], Eric Massicotte[h], Christian Mazel[m], Cumhur Oner[n], Wilco Peul[o], Nasir Quraishi[p], Yasuaki Tokuhashi[q], Katsuro Tomita[r], Christian Ulbricht[s], Jorrit-Jan Verlaan[n], Mike Wang[t], David Choi[a].

Institutions

[a] Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, University College London, London, United Kingdom

[b] Department of Statistical Science, University College London, London, United Kingdom

[c] Department of Neurosurgery, Medical Center Haaglanden, Haaglanden, the Netherlands

[d] Departments of Orthopedic and Neurological Surgery, Washington University, St. Louis, Missouri, United States of America

[e] Department of Neurosurgery, Seoul National University Hospital, Seoul, Republic of Korea

[f] Department of Neurosurgery, University Medical Center Groningen, Groningen, the Netherlands

[g] Division of Neurosurgery, University Hospital Leuven, Leuven, Belgium

[h] Division of Neurosurgery and Spinal Program, University of Toronto and Toronto Western

Hospital, Toronto, Ontario, Canada
[i] Department of Orthopedic Surgery, Kanazawa Medical University Hospital, Kanazawa, Japan
[j] Spine Center, Samsung Medical Center, Seoul, Republic of Korea
[k] Department of Orthopaedics, Musgrove Park Hospital, Taunton, United Kingdom
[l] Spinal Unit, University Hospital Dr Peset, Valencia, Spain
[m] Department of Orthopedic Surgery, Institut Mutualiste Montsouris, Paris, France
[n] Department of Orthopedic Surgery, University Medical Center Utrecht, Utrecht, the Netherlands
[o] Department of Neurosurgery, Leiden University Medical Centre, Leiden, the Netherlands
[p] Centre for Spine Studies and Surgery, Queens Medical Centre, Nottingham, United Kingdom
[q] Department of Orthopaedic Surgery, Nihon University School of Medicine, Japan
[r] Department of Orthopedic Surgery, Kanazawa University, Kanazawa, Japan
[s] Department of Neurosurgery, Charing Cross Hospital, London, United Kingdom
[t] Department of Neurosurgery, University of Miami Hospital, Miami, Florida, United States of America

Corresponding author

David Choi, National Hospital for Neurology and Neurosurgery, Box 3, Queen Square, London, WC1N 3BG, UK. T: +44 3448 3395 F: +44 3448 3340 E: david.choi@nhs.net

Highest academic degrees

Ernest Wright MD

Federico Ricciardi PhD

Mark Arts MD

Jacob M. Buchowski MD

Chun Kee Chung PhD

Maarten Coppes MD

Alan Crockard DSc

Bart Depreitere PhD

Michael Fehlings PhD

Norio Kawahara PhD

Chong Suh Lee MD

Yee Leung FRCS

Antonio Martin-Benlloch MD

Eric Massicotte MD

Christian Mazel MD

Cumhur Oner MD

Wilco Peul MD

Nasir Quraishi FRCS

Yasuaki Tokuhashi MD

Katsuro Tomita MD

Christian Ulbricht FRCS

Jorrit-Jan Verlaan MD

Mike Wang MD

David Choi PhD

Funding Support

This work was funded by the Global Spine Tumour Study Group, a registered charity of England and Wales, Charity Commission number 1134934, and DePuy Synthes (Johnson and Johnson). This study was performed in part at University College London Biomedical Research Centre, which receives funding from the National Institute for Health Research, UK. The authors are members of the Global Spine Tumour Study Group. Other funders had no input in any aspect of the study or manuscript preparation.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

M. Arts

Stock or Other Ownership: Nuvasive, Vexim, Fagron and Pharmine

Consulting or Advisory Role: Amedica, Zimmer Biomet, Silony and EIT

Research Funding: Zimmer Biomet, Amedica, Intrinsics and EIT

Patent, Royalties, other Intellectual Property: EIT

J. Buchowski

Consulting or Advisory Role: Globus Medical

Speakers' Bureau: Globus Medical

Research Funding: Globus Medical

Travel, Accommodations, Expenses: Globus Medical

Patent, Royalties, other Intellectual Property Interest: Globus Medical, K2M and Wolters Kluwer Health

M. Fehlings

Consulting or Advisory Role: Pfizer, Zimmer Biomet and InVivo Therapeutics

C. S. Lee

Consulting or Advisory role: U&I, Korea

Research Funding: Pfizer Korea

Patent, Royalties, other Intellectual property: Solco, Korea and U&I, Korea.

E. Massicotte

Honoraria: AO Spine North America

Travel, Accommodations, Expenses: AO Spine North America

C. Mazel

Stock or Other Ownership: Amplitude

Honoraria: DePuy Spine, Medtronic, Zimmer

Consulting or Advisory Role: Ethicon

Speakers' Bureau: DePuy Spine, Medtronic

Patents, Royalties or other Intellectual Property: CHD

Travel, Accommodations, Expenses: DePuy, Medtronic, Zimmer, Clariance

N. Quraishi

Honoraria: AO Spine, Medtronic, DePuy Synthes

Speakers' Bureau: AO Spine, Medtronic, DePuy Synthes

Travel, Accommodations, Expenses: AO Spine, Medtronic, DePuy Synthes

J. J. Verlaan

Consulting or Advisory Role: DePuy Synthes (inst)

Research Funding: DePuy Synthes (inst)

M. Wang

Stock or Other Ownership: Innovative Surgical Devices, Spinicity

Consulting or Advisory Role: DePuy Spine, AesculapSpine, Jointax, K2M

Research funding: Department of Defence

Patents, Royalties, other Intellectual Properties: Childrens Hospital of LA, DePuy Spine, Springer Publishing, Quality Medical Publishing.

D. Choi

Research Funding: DePuy Synthes (Inst)

All other authors have nothing to disclose.

Keywords

Epidemiology, Metastases, Spine, Surgery, Tumor,

Abbreviations

EQ-5D	Euroqol 5 Dimension 3 Level measure of health related quality of life
GSTSG	Global Spine Tumour Study Group

Abstract

BACKGROUND

Indications for surgery for symptomatic spinal metastases have been better defined in recent years, and suitable outcome measures established, against a changing back-drop of patient characteristics, tumor behavior and oncological treatments. However variations still exist in the local management of patients with spinal metastases. The objective was to review global trends and habits in the surgical treatment of symptomatic spinal metastases, and how this has changed over the last 25 years.

METHODS

A cohort study of consecutive patients undergoing surgery for symptomatic spinal metastases. Data was collected using a secure internet database, in 22 centers across 3 continents. All patients were invited to take part in the study, unless unable or unwilling to give consent.

RESULTS

There was a higher incidence of colonic, liver, and lung carcinoma metastases in Asian countries, and more frequent presentation of breast, prostate, melanoma metastases in the West. Trends in surgical technique were broadly similar across the centers.

Overall survival rates after surgery were 53% (standard error 0.013) at 1 year, 31% (standard error 0.013) at 2 years, and 10% (standard error 0.013) at 5 years after surgery. Survival improved over successive time-periods, with longer survival in patients who received surgery in 2011-2016 compared to earlier time-periods.

CONCLUSION

Surgical habits have been fairly consistent between countries around the world, and over time. However, patient survival has improved in later years, which is perhaps due to medical advances in the treatment of cancer, improved patient selection, or operating earlier in the course of the disease.

Introduction

The contemporary spinal surgeon is becoming increasingly aware of spinal tumors: metastases are the most common neoplasm of the spine and will present in greater numbers as the global population ages.[1] Due to differences in local management protocols, the decision to undergo surgery and choice of specific operations are likely to vary between geographic regions. Published studies examining spinal metastases are largely limited to the experience of single centers utilizing a variety of tumor classification systems and outcomes measures, making it difficult to compare clinical practices.[2-10] As a consequence, the differences in regional variations in the treatment of spinal metastases remain poorly documented.

The Global Spinal Tumour Study Group (GSTSG) maintains an international, prospectively collected dataset on the surgical treatment of spinal metastases employing a standardized classification system of surgical approaches and the EQ-5D health outcome measure to describe functional outcomes.[2,11] Here, we describe the epidemiological characteristics, surgical management, and outcomes of spinal metastatic disease in ten countries throughout four different regions of the world to determine the variation in surgical trends over time and region.

Material and Methods

Inclusion/Exclusion Criteria

Patients diagnosed with spinal metastases between March 1991 and September 2016 at twenty-two referral centers in ten countries throughout Asia (China, Korea and Japan), mainland Europe (Belgium, Denmark, France, the Netherlands, Spain), the United Kingdom, and North America (Canada and the United States) were recruited for entry into the Global Spine Tumour Study

Group database. All patients underwent surgical intervention. Anonymized patient data was entered into the database directly by practitioners. Patients who were unable to provide consent for participation in research or had incomplete follow-up data (date of death or minimum two year follow-up) were excluded from the database. Ethical regulatory approval was obtained at each of the institutions contributing to the GSTSG database; all patients gave informed consent.

Variables

Clinical data collected included primary malignancy type, spinal levels involved, other sites of metastases (both visceral and extraspinal bone metastases), surgical approach, extent of resection performed, surgical details, quality of life at presentation as assessed by EQ-5D, Frankel score and survival. The extent of resection was stratified according to whether debulking, intralesional corpectomy, or complete vertebrectomy was performed. The STROBE reporting guideline has been implemented in writing this manuscript.

Statistical Analysis

Descriptive statistical summary measures were used to assess relevant variables. Mean and standard deviation were calculated for continuous variables while binary and categorical variables were summarized by frequency and percentage. Kaplan-Meier survival estimators were fitted and curves were constructed. Values lower than P=.05 were considered significant. Data analysis was performed using Stata 13 software (StataCorp LLC, Texas USA).

Results

A total of 2148 patients with spinal metastases were admitted to participating referral centers between March 1991 and September 2016 (figure 1). Application of exclusion criteria yielded 2001 study participants (93.2%). The reasons for exclusion were incomplete follow-up in 5 patients (0.2%); insufficient patient details in one patient, and missing information on surgical approach in 141 patients (6.6%). The data was analyzed in four regions: the United Kingdom (UK), mainland Europe, North America, and Asia. The UK was considered in a separate category to mainland Europe due to anecdotal differences in surgical approach and management in comparison to other European centers.

Figure 1

Figure 2

There were substantial differences in the frequency of tumor types reported between Asia and other regions (figure 2). Asian centers diverged from prevailing trends with a higher frequency of colonic, liver, and lung carcinoma metastases, and a lower frequency of breast, prostate, melanoma metastases, and myeloma. Whereas regions outside of Asia reported liver carcinoma metastases in less than 5% of cases, these metastases were seen in Asian centers in 13% of patients. Similarly, lung carcinoma metastases were found in over a quarter (28%) of Asian referrals, despite rates ranging from 10 to 16% elsewhere. By contrast Asian centers had markedly lower rates of breast carcinoma metastases (6%) as compared with other regions, which reported 14-21% of referrals. This trend was also seen in myeloma where the rate in Asian centers (3%) was less than half that seen in mainland Europe and North America (Table 1).

Examining other regions polled revealed a lower incidence in presentation of metastatic prostate cancer in Asia and North America where rates of 5 and 7% (respectively) were substantially lower than those reported in Europe and the UK where it was found in 16-18% of cases. Sarcomas exhibited a unique trend with higher rates in UK and North America (3 and 5% respectively), than in Asia and Mainland Europe (2 and 1 % respectively). Rates of lymphoma, renal, and other uncategorized metastases were similar across all regions.

Despite the differences in frequency of tumor types across regions, there was little variation in the male/female ratio with the percentage of male patients ranging from 55-60% globally (54.9% in the UK, 57.0% mainland Europe, 60.4% in Asia, 59.7% in North America). Similarly, the average age of patients at presentation ranged from 58-62 years across all regions (mean age 61.6 years in UK, 62.0 years Mainland Europe, 60.0 years Asia, 58.1 years in North America).

Table 1

Globally, the majority of surgery was performed via a posterior-only midline approach to the spine. Isolated posterior approaches were employed in 77% (in North America) to 94 % of cases (in Asia). Combined anterior-posterior approaches to the spine, and anterior-only approaches, were the next most common, being employed less than 20% and 10% of the time respectively. Preoperative endovascular tumor embolization was employed in 10-22% of cases worldwide, and was performed in 9.6% of cases in the UK, 14.6% of cases in mainland Europe, 22.1% of cases in Asia, and 16.4% of cases in North America.

Figure 3

Trends in the extent of surgical resection differed between North American centers and other regions. In the UK, Europe, and Asia the majority of cases performed were piecemeal resections with the objective of palliative decompression (defined as <50% of tumor resected, as judged by the surgeon at the time of the operation, figure 3). In North America by contrast palliative decompressions were less frequently performed: the most commonly performed procedure in North American centers was piecemeal debulking of the metastatic lesion with greater than 50% of the lesion resected. For most regions, more palliative and debulking surgeries were performed, rather than complete corpectomies or en bloc resections. North American centers departed from this global trend in that a larger proportion of more aggressive resections were performed. In Asian centers piecemeal vertebrectomy was uncommon. As a result, resections in Asia can be largely dichotomized into piecemeal procedures or en bloc vertebrectomy, revealing a preference for en bloc resection when vertebrectomy was the objective.

The mean case duration differed little between regions, ranging from 3.3 to 3.8 hours globally. The distribution of case duration reveals that most cases were clustered around the overall mean of 3.5 hours in Mainland European (3.3 hours) and North American (3.6 hours) centers, but UK and Asian centers had a substantial proportion of cases that lasted longer than six hours in duration (mean duration 3.7 and 3.8 hours respectively).

Mean duration of stay on the spinal surgery ward varied between regions: In the UK, mean duration was 44 days (standard deviation SD 91 days); on Mainland Europe, mean 29 days

(SD 213 days); in Asia, mean 28 days, (SD 31 days); and in North America, mean duration of stay was 12 days (SD 28 days).

Pre-operative EQ-5D scores were similar between regions outside North America (UK mean EQ-5D score of 0.39, mainland Europe mean 0.40, Asia mean 0.41). North American patients reported significantly higher pre-operative EQ-5D scores with a mean value of 0.51. Standard deviation was consistent for all regions, ranging from 0.28 in North America to 0.32 in Asia.

Survival comparisons

Figure 4

Overall survival rates were 53% (standard error SE=0.013) at one year, 31% (SE=0.013) at two years, and 10% (SE=0.013) at five years (figure 4).

An examination of two-year survival by region (figure 5) revealed that survival in the UK and Mainland Europe differed from that in Asia and North America. ($p<0.05$). Two-year survival in the UK was mean 26% (SE 3.0), mainland Europe was mean 28% (SE 2.0), Asia mean 52% (SE 5.0) and North America mean 42% (SE 4.0).

Figure 5

Figure 6

Dividing study participants into four-year study periods based on year of surgery allowed an analysis of trends over time (figure 6). While one-year survival rates remained largely unchanged, survival rates beyond one year improved in patients diagnosed more recently. Compared to the baseline 1991-2000 group, there was a non-significant improvement in survival in the 2006-2010 group (P=.16), but significant improvements in the 2006-2010 (P=.02) and 2011-2016 groups (P<.01). This is particularly evident for the most recent group of patients recruited between 2011 and 2016 for which the Kaplan-Meier survival curve diverges from those of previous time periods.

The greatest difference in survival over the years was seen in the elderly population (71-80 years group) where there was better survival in elderly patients with metastatic disease in recent years (figure 7). Cox regression models of multiple variables revealed improved survival was related to the age at the time of surgery (P=.004) and the method of surgical tumor excision. Debulking and palliative surgeries were more frequently performed in recent years, and fewer en bloc excisional surgeries are now seen, as surgical philosophy has evolved from curative intent to improvement of quality of life (palliative surgery technique P<.01).

Figure 7

The neurological status at presentation as indicated by Frankel Grade improved over time, with a larger proportion of patients graded as Frankel E and a concomitant decrease in the proportion of Frankel grade C and D patients (table 2: In the 2011-16 group, 44.7% of patients presented with Frankel grade E, but only 25.6% of patients in the 1991-2001 group).

Table 2

The mean age of patients at the time of diagnosis demonstrated little variation across time periods, averaging between 59.6 and 61.0 years of age. The extent of resection varied minimally over time with decompression or simple debulking representing the majority of cases (71.8-100%) and complete vertebrectomy being the objective in only a minority of cases (1.0-16%, table 3). Consistency was also observed in the relative proportions of primary tumor types over time: the three most common tumors reported across all time blocks were breast, renal, and lung carcinoma metastases, excluding cases in which there was no known histopathology (table 4). Analyzing individual tumor types, there was a trend towards better survival in recent years for breast carcinoma metastases (figure 8, P=.18) and colorectal carcinoma metastases (figure 9, P=.13), but not statistically significant perhaps due to small sample size. However there was a significant improvement in survival after surgery for lung cancer (figure 10, P=.04). Other tumor types were not associated with improved survival in recent years.

Figure 8

Figure 9

Figure 10

Table 3

Table 4

Discussion

Regional differences in frequency of tumor types

In this study, the first global comparison of the surgical treatment of spinal metastases, we report wide variation in the frequency of metastatic tumor types between regions. The asymmetries observed in different parts of the world largely reflect those of primary cancer diagnoses in the respective regions. For example, the finding that Asian centers had higher numbers of GI, liver, and lung carcinoma metastases, reflects the high frequency of these primary cancers reported in Asia. Examining regional variations in the incidence of liver cancer in particular: of the over 750,000 new diagnoses of liver cancer made per year, China alone accounts for 50%.[12] In comparison to other regions, the incidence of liver cancer in China is more than three times that in North America and ten times that in some European countries.[12] The relatively small proportion of breast cancer metastases reported in Asian centers lends further support for this explanation, as epidemiological data reveals that the incidence of breast cancer in the United States is a multiple of that reported in most Asian countries.[12]

This explanation however fails to account for certain regional variations seen in our study. Although Asian centers report the single largest proportion of spinal metastases in any region with lung cancer accounting for over a quarter of all spinal metastases, the incidence of primary lung cancer diagnoses is actually lower in China than it is in the United States.[13,14] This unexpected finding may be in part due to early detection initiatives in the United States which call for regular radiographic screening of high risk patients, resulting in diagnosis of asymptomatic patients with isolated lung nodules before metastasis to distant sites can occur.[15,16,17] It is also worth remembering that this study group represents only a subset of patients with spinal metastases in that it is limited to those who have undergone surgery for treatment of their metastatic disease. Consequently, it may be the case that the advent and widespread availability of targeted therapies for lung cancer in the United States is resulting in better medical control and fewer surgical referrals.[18] Taken together, these considerations illustrate that there is no simple or straightforward explanation for the different rates of primary tumors metastasizing to the spine. Rather the interplay between regional primary cancer rates, cancer screening protocols enabling early detection prior to distant spread, and access to advanced oncological therapies, probably contribute to produce the regional variations we report here.

Survival analysis

Examining the results of our survival analysis with respect to the year of diagnosis reveals that long-term survival improved over the time course of this study. Despite the fact that one year survival remained largely unchanged from 1991 to 2016, the Kaplan-Meier survival curve for the most recent quartile (2011-2016) diverged significantly from those representing earlier time periods. The reasons behind this improvement in long-term survival are difficult to determine with certainty, but the fact that the surgical approaches employed and the extent of resection achieved throughout the time periods analyzed remained the same suggests that the improvements demonstrated here are not attributable to differences in surgical treatment. Rather, it is more likely that the gains achieved in long-term survival reflect a combination of earlier detection,[15,16] more efficacious adjuvant medical therapies,[19,20,21,22] and a better understanding of spinal metastatic disease leading to selection of patients better suited for surgery with a greater potential for long term survival.[10] Changes in the medical management of lung cancer are likely to be responsible for better survival in recent years (figure 10), and similar trends were seen in patients with spinal metastases due to breast or colorectal carcinomas (figures 8,9). The improvement in survival in more elderly groups may be due to a combination of better medical treatments and more palliative, less extensive (and therefore complicated) surgeries which have been performed in recent years.

EQ-5D

North American centers reported significantly higher pre-operative EQ-5D scores than in other parts of the world. This finding could be interpreted as evidence of earlier detection, more timely referrals, or a preference for surgical treatment. Alternatively, this may not reflect a genuine functional difference but instead could be attributed to recognized differences in how patients from different regions self-assess well-being. The purpose of country-specific preference weights as applied to the EQ-5D scoring system is to account for known differences in self-assessment and to normalize them to facilitate accurate cross-cultural comparisons. In an examination of US, UK, and Japanese EQ-5D country-specific preference weights as applied to a Thai population of type 2 diabetic patients, Sakthong et al found that application of US preference weights yielded higher scores than the UK or Japanese preference weights.[23] Whether the higher preoperative EQ-5D scores in US patients reported here is artefactual or attributable to genuine differences in practice is difficult to say.

Limitations

Our database is subject to inherent limitations which may impact the generalizability of our conclusions. Given that our dataset is composed exclusively of surgical patients, all non-surgically treated patients were excluded from our analyses. Patients with poor prognoses are typically not considered candidates for surgery, so a focused analysis of surgically treated patients may introduce a selection bias whereby study participants represent a subset of patients with better prognosis than the population of patients with spinal metastases at large. The data in this study was entirely self-reported, and as such is susceptible to reporting bias. This is particularly true for the extent of resection, which was based on each individual surgeon's estimation of the overall percentage of the lesion resected rather than objective radiological criteria. The surgical practice of individual centers may vary, and inclusion of data from units with a preference for more complete or aggressive surgery may bias the results. Lastly, the prospective collection of data over the span of more than a decade means that data was collected at different points in time.

Conclusions

In this first global comparison of the epidemiology, surgical approaches, and long-term survival in patients undergoing surgery for treatment of spinal metastases we find substantial regional variation in the composition of primary tumor types leading to spinal metastatic disease despite uniformity in the preferred surgical approach, surgical objectives, and long-term survival. The regional variation reported here should lend further support for global collaboration, as what is considered a rare metastasis for some may be commonplace for others. On a local scale, this data should prompt surgeons to seek out oncologists with particular expertise in managing the metastases that present most frequently in their region.

The long-term survival data reported here reveals that patients with spinal metastases are living longer. This improvement in long-term survival should prompt reconsideration of our surgical decision-making processes. Many of the prognostic scoring algorithms that we employ in patient selection for surgery were constructed on data gathered more than a decade prior. Given the improved long-term survival we report from 2011-2015, surgeons should be wary of using these prognostic scoring systems, which might exclude patients from surgery on the basis of predictions calculated using old data.

Surgery for spinal metastases can improve pain, deformity, and neurological function.[24] It is well recognized that multidisciplinary team discussion is paramount in formulating treatment strategies that yield the best outcomes for patients. Patients with spinal metastases are now living longer without any change in surgical management, suggesting that this enhanced survival is largely due to advances in medical therapy and radiation techniques. Consequently, the survival benefit reported here should be interpreted as further support for a collaborative approach towards the management of spinal metastases relying on expertise in oncology, surgery, and radiotherapy, to offer an integrated and personalized treatment for patients.

Figure Captions

Figure 1: Consort flow diagram for patient recruitment and exclusion.

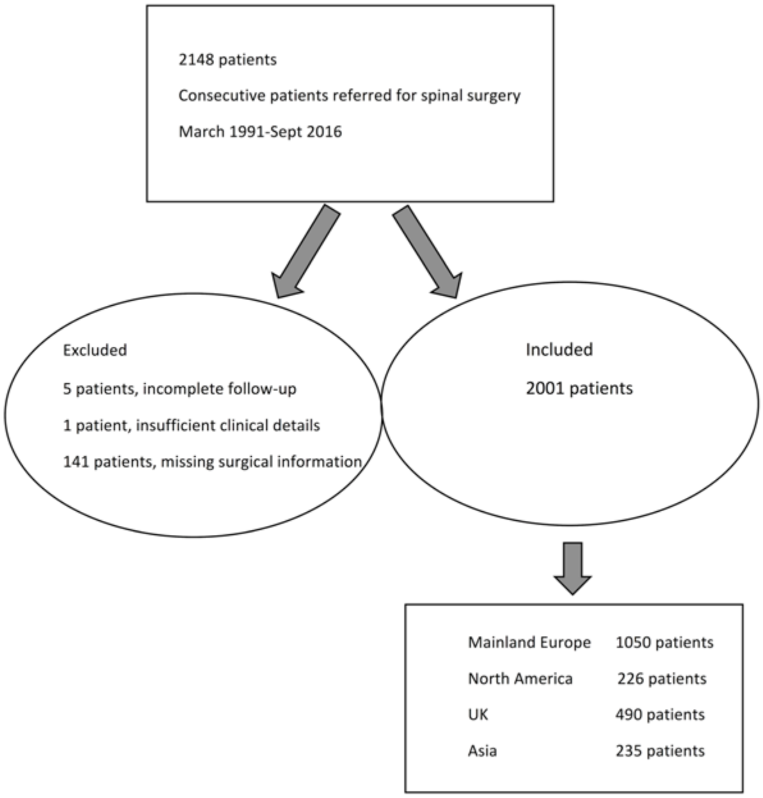

Figure 2: Tumor types in different regions.

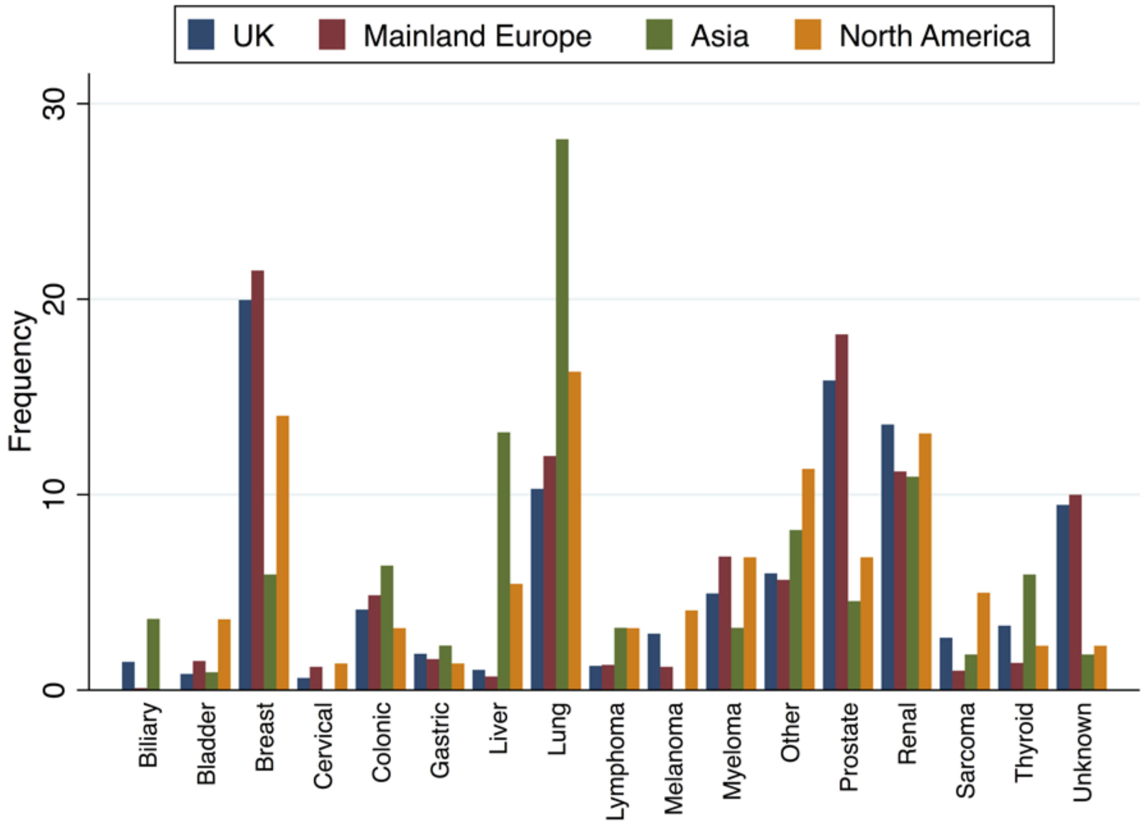

Figure 3: Type of surgery performed in different regions.

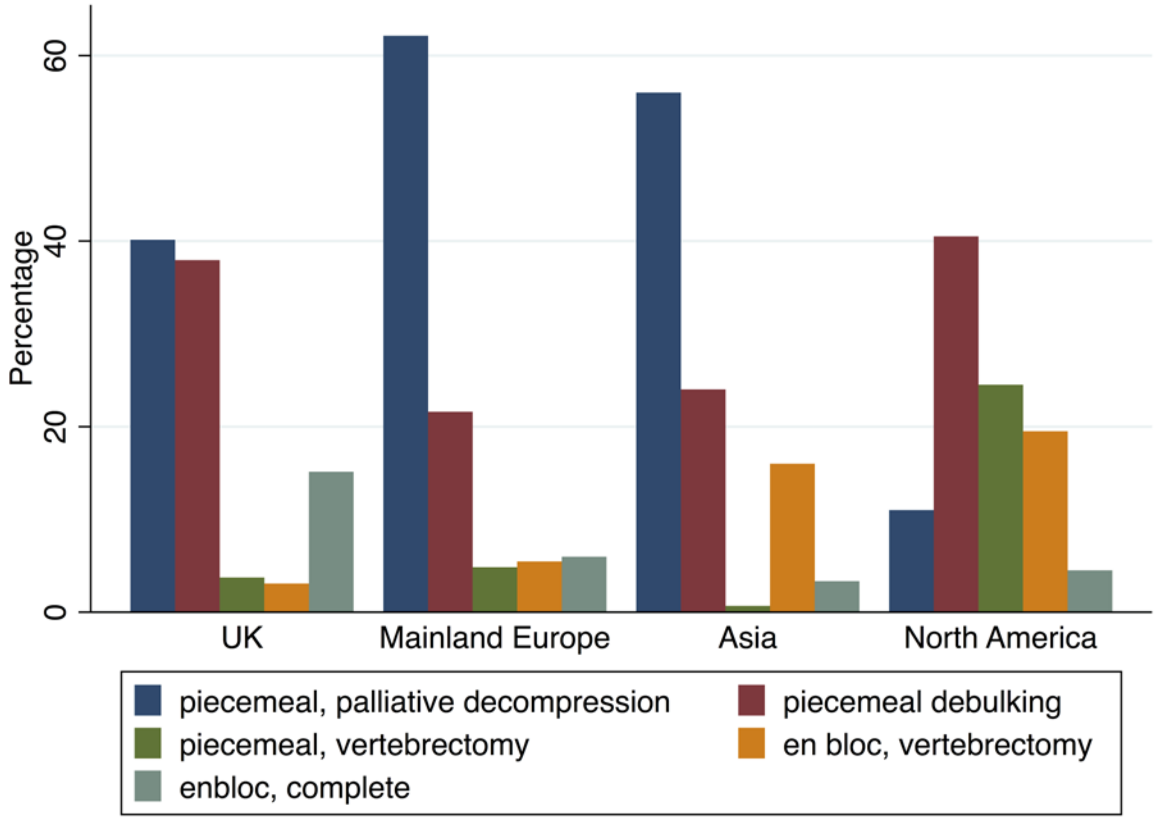

Figure 4: Overall survival after surgery.

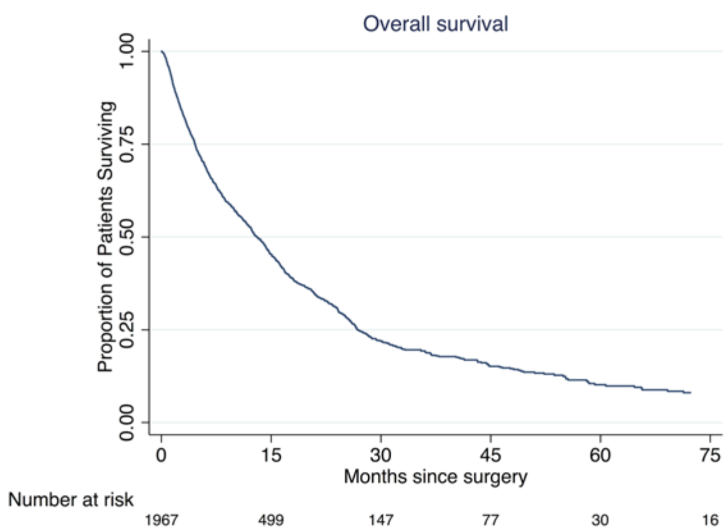

Figure 5: Survival after surgery in different geographical regions.

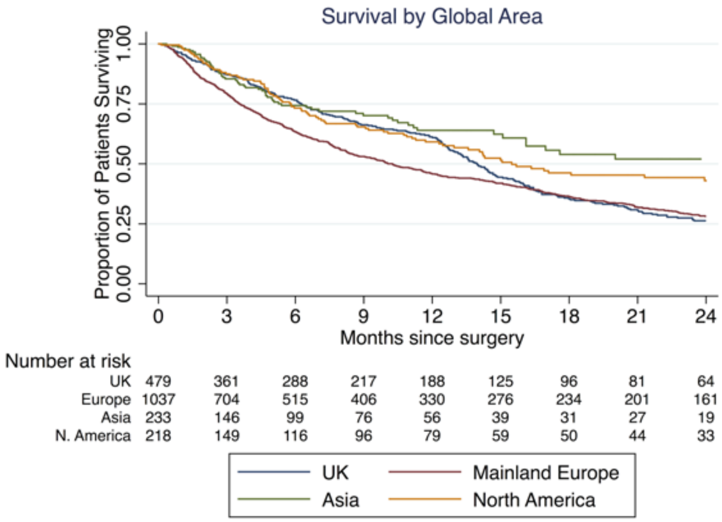

Figure 6: Survival after surgery for successive 5 year recruitment periods, demonstrating improving outcomes.

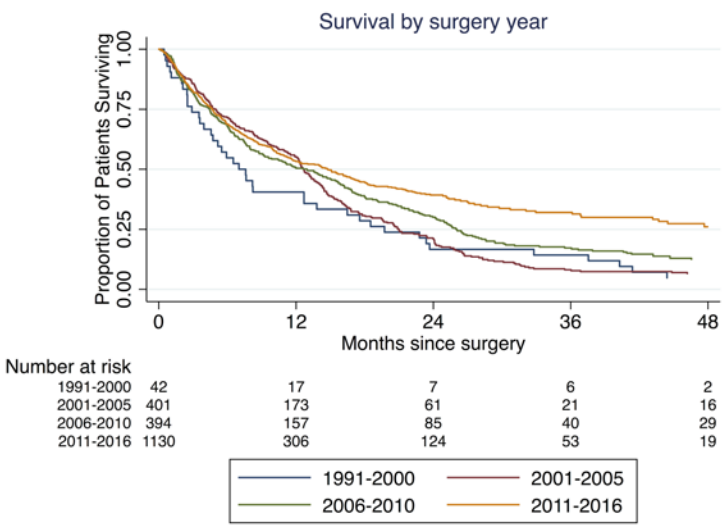

Figure 7: Survival over successive 5 year periods in patients who are aged between 71 and 80 years.

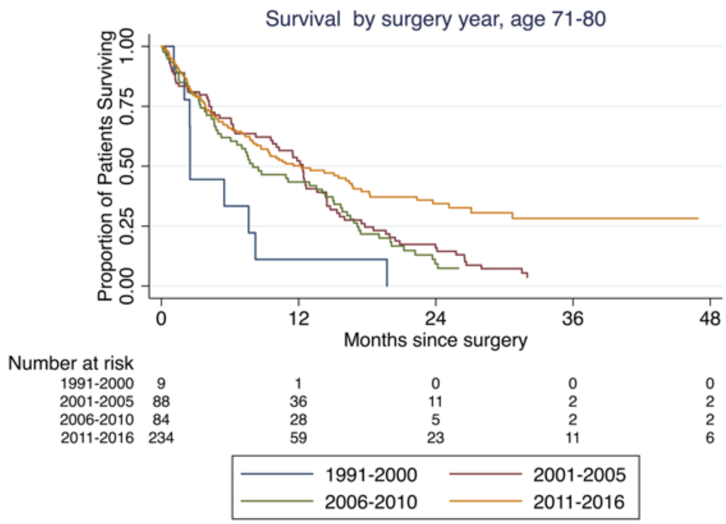

Figure 8: Survival over time, for breast carcinoma metastases to the spine.

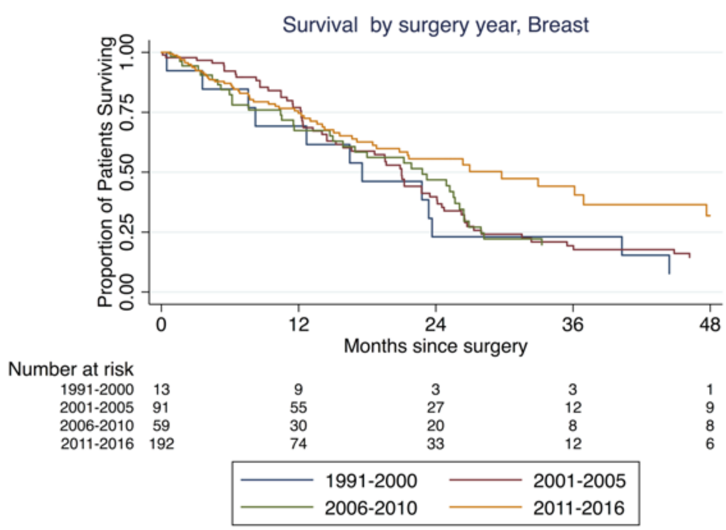

Figure 9: Survival over time, for colorectal carcinoma metastases to the spine.

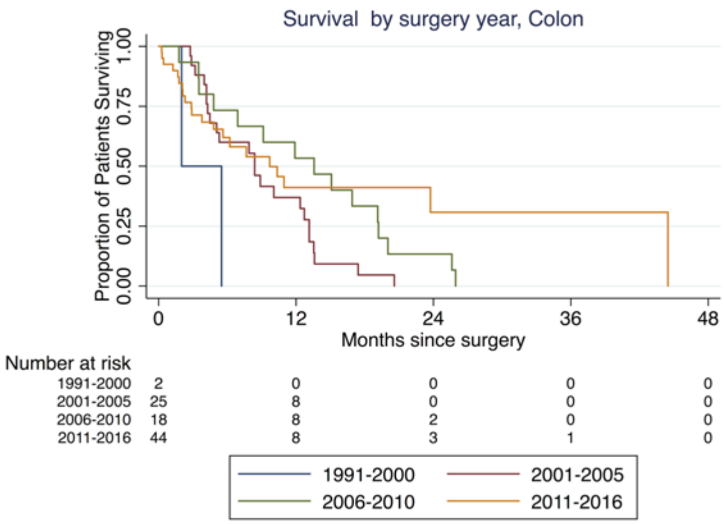

Figure 10: Improved survival over time, for lung cancer metastases to the spine.

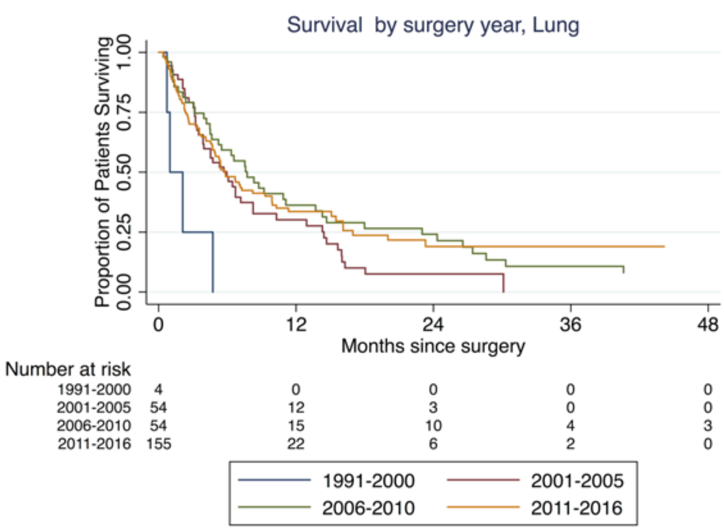

Table Captions

Table 1: Tumor type by global area (numbers and percentages). Missing n=63 (3.2%)

Tumour Type	**UK**	**Mainland Europe**	**Asia**	**North America**	**Total**
Biliary	7 (1.4)	1 (0.1)	8 (3.6)	0 (0)	16 (0.8)

Bladder	4 (0.8)	15 (1.5)	2 (0.9)	8 (3.6)	29 (1.5)
Breast	97 (20.0)	217 (21.5)	13 (5.9)	31 (14.0)	358 (18.5)
Cervical	3 (0.6)	12 (1.2)	0 (0)	3 (1.4)	18 (0.9)
Colon	20 (4.1)	49 (4.9)	14 (6.4)	7 (3.2)	90 (4.6)
Gastric	9 (1.9)	16 (1.6)	5 (2.3)	3 (1.4)	33 (1.7)
Liver	5 (1.0)	7 (0.7)	29 (13.2)	12 (5.4)	53 (2.7)
Lung	50 (10.3)	121 (12.0)	62 (28.1)	36 (16.3)	269 (13.9)
Lymphoma	6 (1.2)	13 (1.3)	7 (3.2)	7 (3.2)	33 (1.7)
Melanoma	14 (2.9)	12 (1.2)	0 (0)	9 (4.1)	35 (1.8)
Myeloma	24 (4.9)	69 (6.8)	7 (3.2)	15 (6.8)	115 (5.9)
Other	29 (6.0)	57 (5.6)	18 (8.2)	25 (11.3)	129 (6.7)
Prostate	77 (15.8)	184 (18.2)	10 (4.6)	15 (6.8)	286 (14.8)
Renal	66 (13.6)	113 (11.2)	24 (10.9)	29 (13.1)	232 (12.0)
Sarcoma	13 (2.7)	10 (1.0)	4 (1.8)	11 (5.0)	38 (2.0)
Thyroid	16 (3.3)	14 (1.4)	13 (5.9)	5 (2.3)	48 (2.5)
Unknown	46 (9.5)	101 (10.0)	4 (1.8)	5 (2.3)	156 (8.1)
Total	486 (100.0)	1011 (100.0)	220 (100.0)	221 (100.0)	1938 (100.0)

Table 2: Frankel grade by year (numbers and percentages). Missing n=14 (0.7%)

Frankel Grade	**1991-2001**	**2001-2005**	**2006-2010**	**2011-2016**	**Total**
A	0 (0.0)	4 (1.0)	8 (2.0)	18 (1.6)	30 (1.5)
B	2 (4.7)	9 (2.3)	18 (4.4)	45 (4.0)	74 (3.7)
C	14 (32.6)	102 (25.6)	81 (20.0)	220 (19.3)	417 (21.0)
D	16 (37.2)	150 (37.7)	144 (35.5)	348 (30.5)	658 (33.1)
E	11 (25.6)	133 (33.4)	155 (38.2)	509 (44.7)	808 (40.7)
Total	43 (100.0)	398 (100.0)	406 (100.0)	1140 (100.0)	1987 (100.0)

Table 3: Extent of excision by year (numbers and percentages). Missing n=189 (9.5%)

Extent of	**1991-2000**	**2001-2005**	**2006-2010**	**2011-2016**	**Total**

Incision					
Cementoplasty	0 (0.0)	0 (0.0)	8 (2.0)	26 (2.7)	34 (1.9)
Palliative Decompression	43 (100.0)	233 (58.4)	182 (46.3)	435 (44.5)	893 (49.3)
Palliative Debulking	0 (0.0)	84 (21.1)	100 (25.5)	316 (32.3)	500 (27.6)
Piecemeal Vertebrectomy	0 (0.0)	5 (1.3)	47 (12.0)	62 (6.4)	114 (6.3)
En-bloc Intralesional	0 (0.0)	12 (3.0)	35 (8.9)	83 (8.5)	130 (7.2)
En-bloc Extralesional	0 (0.0)	65 (16.3)	21 (5.3)	55 (5.6)	141 (7.8)
Total	43 (100.0)	399 (100.0)	393 (100.0)	977 (100.0)	1812 (100.0)

Table 4: Comparison of the presenting tumour types in different time periods (numbers and percentages). Missing n=63 (3.2%)

Tumour Type	**1991-2000**	**2001 - 2005**	**2006 - 2010**	**2011-2016**	**Total**
Biliary	0 (0.0)	6 (1.5)	0 (0.0)	10 (0.9)	16 (0.8)
Bladder	0 (0.0)	6 (1.5)	4 (1.0)	19 (1.7)	29 (1.5)
Breast	13 (30.2)	91 (22.8)	61 (15.3)	193 (17.6)	358 (18.5)
Cervical	1 (2.3)	3 (0.8)	2 (0.5)	12 (1.1)	18 (0.9)
Colon	2 (4.7)	25 (6.3)	19 (4.8)	44 (4.0)	90 (4.6)
Gastric	0 (0.0)	5 (1.3)	4 (1.0)	24 (2.2)	33 (1.7)
Liver	0 (0.0)	6 (1.5)	6 (1.5)	41 (3.7)	53 (2.7)
Lung	4 (9.3)	54 (13.5)	55 (13.8)	156 (14.2)	269 (13.9)
Lymphoma	0 (0.0)	0 (0.0)	6 (1.5)	27 (2.5)	33 (1.7)
Melanoma	0 (0.0)	7 (1.8)	7 (1.8)	21 (1.9)	35 (1.8)
Myeloma	1 (2.3)	1 (0.3)	35 (8.8)	78 (7.1)	115 (5.9)
Other	1 (2.3)	17 (4.3)	26 (6.5)	85 (7.8)	129 (6.7)
Prostate	8 (18.6)	68 (17.0)	70 (17.6)	140 (12.8)	286 (14.8)
Renal	6 (14.0)	52 (13.0)	48 (12.1)	126 (11.5)	232 (12.0)
Sarcoma	0 (0.0)	1 (0.3)	7 (1.8)	30 (2.7)	38 (2.0)
Thyroid	2 (4.7)	12 (3.0)	13 (3.3)	21 (1.9)	48 (2.5)
Unknown	5 (11.6)	46 (11.5)	35 (8.8)	70 (6.4)	156 (8.1)

Total	43 (100.0)	400 (100.0)	398 (100.0)	1097 (100.0)	1938 (100.0)

References

1. Godersky JC, Smoker WR, Knutzon R. Use of magnetic resonance imaging in the evaluation of metastatic spinal disease. *Neurosurgery*. 1987;21:676-680.
2. Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamara T. Surgical Strategy for Spinal Metastases. *Spine*. 2001;26:298-306.
3. North RB, LaRocca VR, Schwartz J, et al. Surgical management of spinal metastases: analysis of prognostic factors during a 10-year experience. *Journal of Neurosurgery: Spine*. 2005;2:564-573.
4. Gerszten PC, Burton SA, Ozhasoglu C, Welch WC. Radiosurgery for Spinal Metastases: Clinical Experience in 500 Cases From a Single Institution. *Spine.* 2007;32:193-199.
5. Tokuhashi Y, Matsuzaki H, Oda H, Oshima M, Ryu J. A Revised Scoring System for Preoperative Evaluation of Metastatic Spine Tumor Prognosis. *Spine.* 2005;30:2186-2191.
6. Hirabayashi H, Ebara S, Kinoshita T, et al. Clinical outcome and survival after palliative surgery for spinal metastases. *Cancer*. 2003;97:476–484.
7. Jansson KÅ, Bauer HCF. Survival, complications and outcome in 282 patients operated for neurological deficit due to thoracic or lumbar spinal metastases. *Eur Spine J.* 2006;15:196-202.
8. Bauer HCF, Wedin R. Survival after surgery for spinal and extremity metastases: Prognostication in 241 patients. *Acta Orthopaedica Scandinavica.* 1995;66:143-146.
9. Wise JJ, Fischgrund JS, Herkowitz HN, Montgomery D, Kurz LT. Complication, Survival Rates, and Risk Factors of Surgery for Metastatic Disease of the Spine. *Spine. 1999;*24:1943.

10. Wang MY, Parr AM. An International Initiative to Define the Role for Surgery for Spinal Metastases: The GSTSG. *World Neurosurgery*. 2010;73:426-427.

11. Choi D, Morris S, Crockard A, et al. Assessment of Quality of Life After Surgery for Spinal Metastases: Position Statement of the Global Spine Tumour Study Group. *World Neurosurgery*. 2013;80:e175-e179.

12. American Cancer Society. *Global Cancer Facts & Figures 3rd Edition*. Atlanta: American Cancer Society; 2015.

13. Youlden DR, Cramb SM, Baade PD. The International Epidemiology of Lung Cancer: Geographical Distribution and Secular Trends. *Journal of Thoracic Oncology*. 2008;3:819-831.

14. Gibberd R. Globocan 1: Cancer Incidence and Mortality Worldwide. J. Ferlay, D.M. Parkin and P.Pisani, IARC Press, Lyon, 1999. *Statistics in Medicine*. 2000;19:2714-2715.

15. Moyer VA. Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine*. 2014;160:330-338.

16. Pastorino U, Bellomi M, Landoni C, et al. Early lung-cancer detection with spiral CT and positron emission tomography in heavy smokers: 2-year results. *Lancet*. 2003;362:593-597.

17. National Lung Screening Trial Research Team. Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening. *New England Journal of Medicine*. 2011;365:395-409.

18. Rolfo C, Passiglia F, Ostrowski M, et al. Improvement in Lung Cancer Outcomes With Targeted Therapies: An Update for Family Physicians. *The Journal of the American Board of Family Medicine*. 2015;28:124-133.

19. International Early Lung Cancer Action Program Investigators. Survival of Patients with Stage I Lung Cancer Detected on CT Screening. *N Engl J Med.* 2006;355:1763-1771.

20. Smith I, Procter M, Gelber RD, et al. 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomised controlled trial. *The Lancet*. 2007;369:29-36.

21. Early Breast Cancer Trialists' Collaborative Group. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *The Lancet.* 2005;365:1687-1717.

22. Chia SK, Speers CH, D'yachkova Y, et al. The impact of new chemotherapeutic and hormone agents on survival in a population-based cohort of women with metastatic breast cancer. *Cancer*. 2007;110:973-979.

23. Sakthong P, Charoenvisuthiwongs R, ShabunthomR. A comparison of EQ-5D index scores using the UK, US, and Japan preference weights in a Thai sample with type 2 diabetes. *Health and Quality of Life Outcomes. 2008;*6:71.

24. Choi D, Fox Z, Albert T, et al. Rapid improvements in pain and quality of life are sustained after surgery for spinal metastases in a large prospective cohort. *British Journal of Neurosurgery.* 2016;30:337-344.