

# Spondylectomy in the treatment of neoplastic spinal lesions – A retrospective outcome analysis of 582 patients using a patient-level meta-analysis

## ABSTRACT

This study aims at identifying predictors of postoperative complications, lesion recurrence, and overall survival in patients undergoing en bloc spondylectomy (EBS) for spinal tumors. For this purpose a systematic review of the literature was conducted and patient-level data extracted. Linear-regression models were calculated to predict postoperative complications, lesion recurrence and overall survival based on age, tumor etiology, surgical approach, mode of resection (extra- vs. intralesional), tumor extension, and number of levels treated. A total of 582 patients were identified from the literature: 45% of females, median age 46 years (5–78); most common etiologies were: sarcoma (46%), metastases (31%), chordoma (11%); surgical approach was anterior (2.5%), combined (45%), and posterior (52.4%); 68.5% underwent EBS; average levels resected were 1.6 (1–6); average survival was 2.6 years; Complication rate was 17.7%. The following significant correlations were found: postoperative complications and resection mode (Odds ratio [OR] 1.35) as well as number of levels treated (OR 1.35); tumor recurrence and resection mode (OR 0.78); 5-year survival and age (OR 0.79), tumor grade (OR 0.65), tumor stage at diagnosis (OR 0.79), and resection mode (OR 1.68). EBS was shown to improve survival, decreases recurrence rates but also has a higher complication rate. Interestingly, the complication rate was not influenced by tumor extension or tumor etiology.

**Keywords:** Spinal aneurysmal bone cyst, spinal chordoma, spinal giant cell tumor, spinal sarcoma, spondylectomy

## INTRODUCTION

The surgical resection of an entire vertebral body, termed spondylectomy, can be indicated in the treatment of certain primary as well as secondary spinal tumors. Since the vertebral body periosteum, anterior longitudinal ligament, ligamentum flavum and to a lesser extend the posterior longitudinal ligament are considered barriers in the spread of vertebral tumors, an extralesional, total *en bloc* spondylectomy (TES) has been shown to result in superior oncologic outcomes in a variety of conditions, mainly primary spinal tumors.

While previous studies have clearly shown the superior oncologic outcome of TES over intralesional resections in the treatment of chordoma,<sup>[1]</sup> high-grade sarcoma<sup>[2,3]</sup> or giant cell

**ALEXANDER SPIESSBERGER<sup>1,2</sup>, NICHOLAS DIETZ<sup>3</sup>, VARUN ARVIND<sup>1</sup>, MANSOOR NASIM<sup>4</sup>, BASIL GRUTER<sup>5</sup>, EDIN NEVZATI<sup>6</sup>, SILVIA HOFER<sup>7</sup>, SAMUEL K CHO<sup>1</sup>**

<sup>1</sup>Department of Orthopedic Surgery, Icahn School of Medicine - Mount Sinai Hospital, <sup>2</sup>Department of Neurosurgery, Hofstra School of Medicine, North Shore University Hospital, <sup>4</sup>Department of Pathology and Laboratory Medicine, Zucker School of Medicine at Hofstra Northwell, NY, <sup>3</sup>Department of Neurosurgery, University of Louisville, Louisville, KY, USA, <sup>5</sup>Department of Neurosurgery, University Hospital Zurich, Zurich, Departments of <sup>6</sup>Neurosurgery and <sup>7</sup>Medical Oncology, Cantonal Hospital of Lucerne, Lucerne, Switzerland

**Address for correspondence:** Dr. Alexander Spiessberger, Department of Neurosurgery, North Shore University Hospital, 300 Community Drive, Manhasset, NY - 11030, USA.  
E-mail: alexander.s.spießberger@gmail.com

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tumor (GCT),<sup>[4]</sup> the role of TES in the treatment of other tumor etiologies, such as aggressive hemangioma,<sup>[5]</sup> desmoplastic fibroma,<sup>[6]</sup> osteoblastoma,<sup>[7]</sup> or aneurysmal bone cyst (ABC)<sup>[8,9]</sup> is poorly defined.

The technique of TES was first described by Roy-Camille *et al.*,<sup>[10]</sup> Stener,<sup>[11]</sup> and later by Tomita *et al.*<sup>[12]</sup> Depending on the anatomic level and tumor extension, either anterior, posterior, or a combined approach is indicated. Surgical decision-making and planning is in part based on the Weinstein-Boriani-Biagini (WBB) tumor classification [Figure 1].<sup>[13,14]</sup>

Since TES is a technically demanding procedure with potential complications such as major vascular or neurologic injury, we aim to define predictors of poor surgical outcomes and postoperative complications to improve patient selection for this procedure. This study is a retrospective multivariate analysis.

### MATERIALS AND METHODS

A systematic review of the literature according to the PROCESS guidelines<sup>[15]</sup> was performed using Medline [Figure 2]. Local ethics committee approval was not necessary for this study.

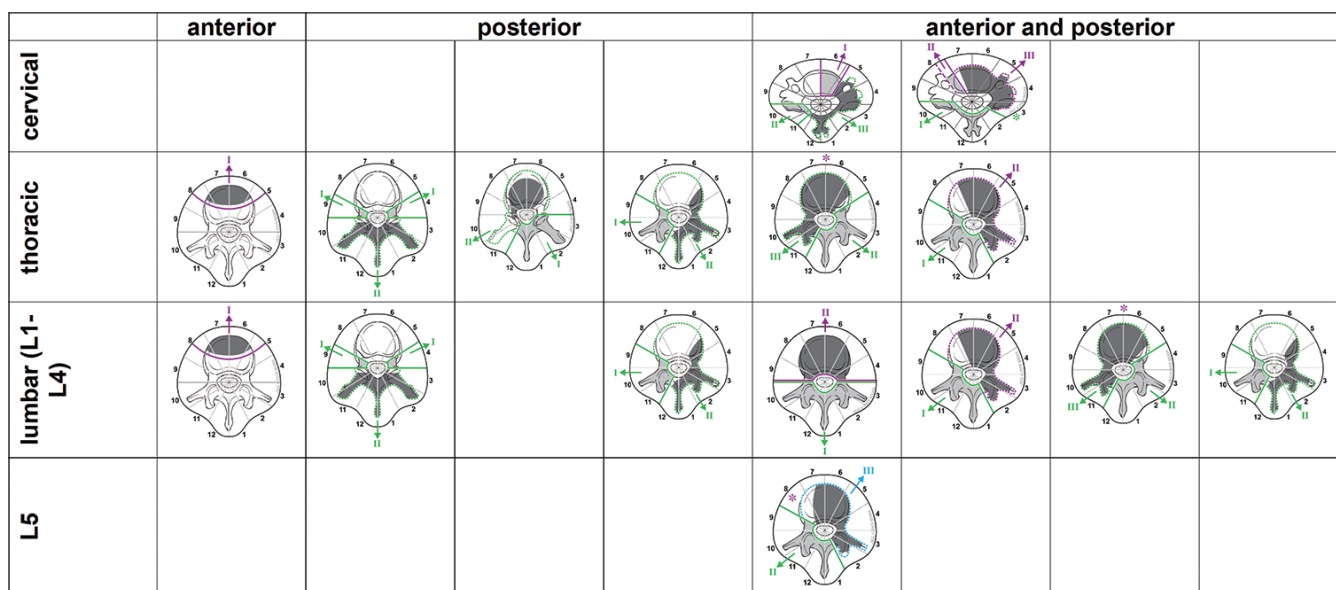
We identified all studies published within Medline until November 16, 2018 utilizing the key word “spondylectomy.”

Exclusion criteria included case reports, nonEnglish language, absence of clinical data, or individual patient data.

For each patient, in all included studies, we extracted the following data: sex, age, tumor etiology, tumor dissemination at diagnosis, surgical approach type (anterior, anterior/posterior, posterior), extralesional or intralesional resection, tumor extension according to WBB classification system,<sup>[16]</sup> anatomic levels treated, duration of procedure (minutes), blood loss (ml), directly procedure-related complications (excluding medical complications and late hardware failure), preoperative neurologic grade (Frankel grade), postoperative neurologic grade (Frankel grade), local recurrence (yes/no), final follow-up (years), and death upon final follow-up (yes/no).

Three separate linear regression analyses were performed using PSPP (Version 1.2.0, GNU Project, Boston, MA) to predict the occurrence of postoperative procedure-related complications, local recurrence, and 5-year survival rate.

Dependent variable in the linear regression model for the occurrence of postoperative complications were categorized as follows: age <18, 18–44, 45–64, >65 years; hypervascular versus nonhypervascular tumor etiology (hypervascular etiologies: metastases of hepatocellular, renal or thyroid carcinoma; hemangioma; hemangiopericytoma; ABC); approach type (anterior, posterior and combined); type of resection (extralesional vs. intralesional resection); tumor morphology according to the WBB classification system: superficial versus deep location in relation to the spinal canal (A, B, C vs. D), size of lesion (tumor occupation of 1–3, 4–6, 7–9, and 10–12 sectors); and number of levels treated.



**Figure 1: Algorithm for total en-bloc spondylectomy based on tumor extension according to the WBB classification system. Dark grey areas indicate tumor extension within a vertebral body, light grey areas indicate areas resected in a piecemeal fashion, while the remaining vertebral body is resected en-bloc. Latin numerals indicate distinct surgical steps, green: posterior resection, purple: anterior resection, blue: lateral retroperitoneal resection; \*Indicated areas of the vertebral body, which are dissected and separated from surrounding structures**

In the linear regression model for local recurrence dependent variables were categorized as follows: etiology (Group 1: ABC, chordoma, desmoplastic fibroma, GCT, aggressive hemangioma, neurofibroma, osteoblastoma; Group 2: hemangiopericytoma, desmoid; Group 3: angiosarcoma, chondrosarcoma, Ewing sarcoma, fibrosarcoma, leiomyosarcoma, undifferentiated pleomorphic sarcoma, neurofibrosarcoma, osteosarcoma, Paget sarcoma, pleomorphic sarcoma, synovial sarcoma, undifferentiated sarcoma, primary invading lung cancer, malignant peripheral nerve sheath tumor, plasmocytoma; Group 4: metastases),<sup>[17]</sup> type of resection (extralesional vs. intralesional resection); tumor morphology according to the WBB classification: superficial versus deep location in relation to the spinal canal (A, B, C, vs. D), size of lesion (tumor occupation of 1–3, 4–6, 7–9, and 10–12 sectors); number of levels treated.

Categorization of dependent variables for the ANOVA model for 5-year survival rate was: age < 18, 18–44, 45–64, >65 years; etiology (Group 1: ABC, chordoma, desmoplastic fibroma, GCT, aggressive hemangioma, neurofibroma, osteoblastoma; Group 2: hemangiopericytoma, desmoid; Group 3: angiosarcoma, chondrosarcoma, Ewing sarcoma, fibrosarcoma, leiomyosarcoma, undifferentiated pleomorphic sarcoma, neurofibrosarcoma, osteosarcoma, Paget sarcoma, pleomorphic sarcoma, synovial sarcoma, undifferentiated sarcoma, primary invading lung cancer, malignant peripheral nerve sheath tumor, plasmocytoma; Group 4: metastases);<sup>[17]</sup> dissemination at diagnosis; type of resection (extralesional vs. intralesional resection).

## RESULTS

The systematic review of literature identified a total of 42 studies, which are listed in Appendix 1. From 42 studies, data were extracted for 582 patients [Table 1], with a median age of 46 years old (range: 5 to 78 years), with 45% of patients being female. The majority of patients had TES (58%) from a posterior-only approach (38.8%). The median number of levels treated was 1, range 1 to 6. At a median of 3.2 years follow-up, 20.6% of patients were dead. Most lesions were located in the thoracic spine (49.7%), followed by the lumbar (26.8%) and cervical spine (21.7%), as shown in Table 2. A detailed list of pathologic diagnoses is given in Table 3, with the most frequent entities being sarcoma, metastases and GCT.

Details of surgery are outlined in Table 1. The median operating time was 555 min with a median blood loss of 2000ml. Local recurrence overall was observed to be 18%. At a median follow-up time of 3.2 years 79.4% of patients were still alive.

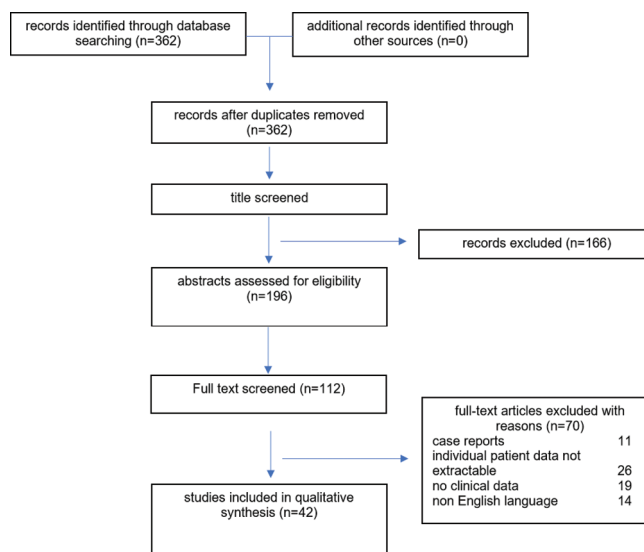


Figure 2: Literature search algorithm

Table 1: Characteristics of patient demographics and procedure details

	Median, range, SD
<i>n</i>	582
Age (years)	46, 5-78, 16.3
Sex, female (%)	263 (45.2)
Approach (a, a/p, p) (%)	1 (0.7), 193 (33.1), 225 (38.8)
TES (%)	338 (58)
Levels	1, 1-6, 0.96
OR time (min)	555, 232-1516, 273.7
Blood loss (ml)	2000, 150-19225, 2494.3
Local recurrence (%)	105 (18)
Follow-up (years)	3.2, 0.008-19.4, 3.5
Dead upon last follow-up (%)	102 (20.6)

TES – Total en-bloc spondylectomy, SD – Standard deviation

Table 2: Anatomic distribution of surgically treated lesions

Level	Lesions, <i>n</i> (%)
Cervical	202 (21.7)
Thoracic	462 (49.7)
Lumbar	249 (26.8)

Directly procedure related complications were observed in 103 patients (17.7%), [Table 4]. The most frequently observed complications were cerebrospinal fluid leak, wound dehiscence, infection, and spinal cord injury.

Results of the multivariate analyses for three dependent variables are shown in Tables 5-7 and significant findings are: odds ratio (OR) for postoperative complications was 1.35 for spondylectomy and 1.25 for number of levels treated. No significant association was found for age, tumor etiology, approach type, or WBB grade. The OR for recurrence was 0.78 for spondylectomy. No association was found for tumor

**Table 3: Tumor entities included in the study**

Etiology	Subtype	Patients	Total patients, n (%)
Sarcoma	Giant cell tumor	114	263 (45.8)
	Osteosarcoma	64	
	Hemangiopericytoma	24	
	Chondrosarcoma	22	
	Desmoplastic fibroma	13	
	Ewing sarcoma	9	
	Undifferentiated sarcoma	5	
	Synovial sarcoma	3	
	Pleomorphic sarcoma	2	
	Angiosarcoma	1	
	Desmoid	1	
	Fibrosarcoma	1	
	Leiomyosarcoma	1	
	Malignant peripheral nerve sheath tumor	1	
	Neurofibrosarcoma	1	
Paget sarcoma	1		
Metastasis	Renal	44	180 (30.9)
	Thyroid	34	
	Breast	26	
	Paraganglioma	16	
	Lung (not further specified)	14	
	Sarcoma	13	
	Adeno carcinoma (not further specified)	7	
	Prostate	5	
	Squamous cell (not further specified)	4	
	Germ cell tumor	3	
	Hepatocellular	2	
	Rectum	2	
	Unknown	2	
	Adrenal	1	
	Cholangiocellular	1	
	Colon	1	
	Endometrium	1	
	Laryngeal	1	
	Malignant schwannoma	1	
	Maxilla	1	
Parotid	1		
Testicular (not further specified)	1		
Chordoma			62 (10.6)
Plasmocytoma			29 (5)
Osteoblastoma			22 (3.8)
Hemangioma			14 (2.4)
Aneurysmal bone cyst			3 (0.5)
Primary invading lung tumor			1 (0.2)
Neurofibroma			1 (0.2)

etiology, tumor extension based on WBB classification system and number of lesions treated. The following OR s for 5-year survival were observed: age 0.79, tumor etiology 0.65, dissemination at diagnosis 0.79, and *en bloc* resection 1.68.

## DISCUSSION

The challenge for spine surgeons remains to select patients who will benefit from TES. As shown in Table 3, the most frequent lesions undergoing TES were sarcoma, metastasis, chordoma, and plasmocytoma. The literature clearly shows, that TES results in superior oncologic outcome in terms of progression free and overall survival for the following

entities: sarcoma,<sup>[18]</sup> GCT,<sup>[19-21]</sup> chordoma<sup>[22]</sup> and ABC.<sup>[23]</sup> In a recent consensus statement by the Chordoma Global Consensus group,<sup>[11]</sup> it was agreed that extralesional resection is the treatment of choice for localized chordoma whenever feasible. R0 resection with adequate margins is the only curative treatment with- or without perioperative radiation in osteosarcoma.<sup>[2,24]</sup> This is contrary to plasmocytoma where the primary treatment is nonsurgical, unless there is mechanical instability, significant deformity or neurologic compromise, as this tumor entity is highly radio- and chemosensitive.

The choice of the appropriate therapeutic approach for spinal metastases requires consideration of several factors

including mechanical instability, deformity, neurologic compromise, as well as local tumor control, especially in solitary lesions or oligometastatic disease. Effective local tumor therapies (i.e., surgical removal or stereotactic radiotherapy, [SRT]) have been shown to prolong survival in different cancer types with solitary lesions (e.g., colorectal, breast, or lung cancer).<sup>[25-27]</sup> This also is reflected in the fact

that metastasis was the second most frequent treatment indication in this study [Table 3]. In recent years, a “less extensive” surgical approach has been proposed, combined with postoperative SRT for patients with spinal metastases and high-grade spinal cord compression. The only indication for surgery with this approach is preservation or restoration of mechanical stability and a circumferential decompression of the spinal cord, whereas the primary goal of SRT is ablation of tumor tissue within the vertebral body.<sup>[28]</sup> The rationale of a less invasive surgical approach is to reduce blood loss and time of surgery, which is of particular importance in patients with more extensive disease.<sup>[29,30]</sup> Second, SRT might result in similar local tumor control rates as surgical resection in malignant lesions. In a recent systematic review by Husain et al.<sup>[31]</sup> analyzed 14 studies with a of 816 patients with spinal metastases; N-weighted average control rate was 87.6% and n-weighted overall survival was 18.2% at a follow-up time of 18.4 month. Laufer et al.<sup>[32]</sup> applied the hybrid concept of separation surgery (surgical “separation” of thecal sac and surrounding tumor tissue) in conjunction with SRT in 186 patients and achieved a local tumor control rate of 83.6% at 1 year. The authors unfortunately do not report

**Table 4: Directly procedure related complications**

Complication	n (%)
CSF leak	30 (5.2)
Wound dehiscence or infection	21 (3.6)
Cord injury	17 (2.9)
Radiculopathy (other than “intentional nerve root sacrifice”)	10 (1.7)
Early hardware failure, migration, malposition	5 (0.8)
Pleural tear	5 (0.8)
Dysphagia	4 (0.7)
Pleural effusion	3 (0.5)
Chylothorax	2 (0.3)
Others	2 (0.3)
Visceral injury	2 (0.3)
Recurrent laryngeal nerve paly	1 (0.2)
Vacular injury	1 (0.2)

CSF – Cerebrospinal fluid

**Table 5: Multivariate linear regression analysis for postoperative complications**

	Unstandardized coefficients		Standardized coefficient (β)	t	OR	Significance
	B	SE				
Age	0.07	0.05	0.14	1.32		0.191
Etiology	-0.04	0.13	-0.04	-0.33		0.745
Approach	-0.05	0.07	-0.08	-0.74		0.462
En bloc	0.22	0.08	0.3	2.62	1.35	0.01
WBB depth	0.03	0.08	0.04	0.33		0.743
WBB size	0.01	0.05	0.03	0.26		0.799
Number of levels	0.09	0.04	0.22	2.2	1.25	0.031

SE – Standard error, OR – Odds ratio, WBB – Weinstein-Boriani-Biagini

**Table 6: Multivariate linear regression analysis for tumor recurrence**

	Unstandardized coefficients		Standardized coefficient (β)	t	OR	Significance
	B	SE				
Etiology	0.04	0.04	0.09	1.01		0.314
En bloc	-0.23	0.08	-0.24	-2.80	0.78	0.006
WBB depth	0.00	0.08	0.00	-0.06		0.953
WBB size	0.05	0.05	0.10	1.21		0.23
Number of levels	-0.04	0.05	-0.07	-0.8		0.423

SE – Standard error, OR – Odds ratio, WBB – Weinstein-Boriani-Biagini

**Table 7: Multivariate linear regression analysis for 5-year survival**

	Unstandardized coefficients		Standardized coefficient (β)	t	OR	Significance
	B	SE				
Age	-0.14	0.05	-0.23	-2.69	0.79	0.008
Etiology	-0.17	0.03	-0.43	-4.82	0.65	0.001
Dissemination	-0.23	0.08	-0.23	-2.8	0.79	0.006
En bloc	0.56	0.09	0.52	6.04	1.68	0.001

SE – Standard error, OR – Odds ratio



surgical details, such as blood loss, duration of surgery, and time to ambulation or complications. Cofano *et al.*<sup>[33]</sup> reported their results of separation surgery in 9 patients with an average blood loss 580 ml and procedure duration of 260 min. Nasser *et al.*<sup>[34]</sup> achieved similar results in 17 patients undergoing separation surgery with an average blood loss of 458 ml and average duration of surgery 408 min. It has to be mentioned, however, that a more complete removal of the diseased vertebral body can be performed using a minimally invasive techniques, as shown by Deutsch *et al.*<sup>[35]</sup> where a minimally invasive partial corpectomy was performed on eight patients with an average blood loss of 227 ml and average operating duration of 2.2h.

Interestingly, attempts have been made in the recent past to perform a TES by means of less invasive surgical approaches, minimizing blood loss, and length of surgical incisions. Turner *et al.*<sup>[36]</sup> performed a mini-open direct lateral TES, unfortunately no data on operative blood loss and duration of surgery are available. A different technique has been described by Xiong *et al.*<sup>[37]</sup> utilizing a paraspinous muscle splitting approach with an average blood loss of 1280 ml (per level).

The only variables correlating with operative complications in our analysis, was extra- versus intralesional tumor resection and increasing number of levels treated. Interestingly, neither tumor entity (dichotomized by vascularity, hyper- or nonhypervascular etiologies) nor tumor grade based on WBB classification system had an association with complication rate, a finding that has not been described before.

Our analysis of 582 patients who underwent surgery for a spinal tumor showed that *en bloc* spondylectomy (EBS) has been shown to positively impact 5 year survival.

Limitations of our analysis are its retrospective nature, inclusion of operative data of many different, high- and low-volume surgical centers with their own in-house policy of technical approaches for spinal tumors, and lack of information about use of adjuvant therapy. Past research has led to the establishment of TES primarily in treatment sarcomatous lesions and chordomas.<sup>[1-3,5,13]</sup> This study confirmed the positive association of extra- versus intralesional resection on recurrence rate and 5-year survival rate. However, we also observe a negative association between EBS and rate of operative complications when compared to intralesional resections. Tumor extension based on WBB classification system, approach type, or tumor histology had no influence on postoperative complications, however increasing number of levels resected was associated with an increased risk of

complications. Long-term survival was negatively impacted by increasing patient age, tumor dissemination and higher tumor grade; however, spondylectomy had a positive association with long-term survival. Future research in spinal surgery should focus on the refinement of surgical approaches to improve long-term survival and decrease risk of procedure-related complications.

## CONCLUSION

This retrospective analysis of 582 patients with spine lesions of benign and malignant etiology reveals that in properly selected patients EBS can be performed with a low risk of serious neurologic complications throughout the mobile spine. Tumor extension based on the WBB classification system and tumor etiology did not increase the risk of complications, however increasing number of levels resected did. We confirm previous findings of significantly decreased recurrence rate and increased 5-year survival rate in patients undergoing EBS.

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## Conflicts of interest

There are no conflicts of interest.

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**Appendix 1: List of studies included in analysis**

Article number	First author	Year of publication	Number of patients
1	Abe <i>et al.</i> <sup>[1]</sup>	2001	14
2	Akeyson and McCutcheon <sup>[2]</sup>	1996	25
3	Balke <i>et al.</i> <sup>[3]</sup>	2012	2
4	Chou <i>et al.</i> <sup>[4]</sup>	2009	3
5	de Carvalho <i>et al.</i> <sup>[5]</sup>	2016	1
6	Demura <i>et al.</i> <sup>[6]</sup>	2011	10
7	Disch <i>et al.</i> <sup>[7]</sup>	2011	20
8	Feng <i>et al.</i> <sup>[8]</sup>	2013	16
9	Guo <i>et al.</i> <sup>[9]</sup>	2011	6
10	Hasegawa <i>et al.</i> <sup>[10]</sup>	2007	13
11	Hsieh <i>et al.</i> <sup>[11]</sup>	2011	5
12	Huang <i>et al.</i> <sup>[12]</sup>	2010	20
13	Huang <i>et al.</i> <sup>[13]</sup>	2018	9
14	Jia <i>et al.</i> <sup>[14]</sup>	2018	13
15	Jia <i>et al.</i> <sup>[15]</sup>	2018	15
16	Jia <i>et al.</i> <sup>[16]</sup>	2018	20
17	Junming <i>et al.</i> <sup>[17]</sup>	2008	21
18	Kato <i>et al.</i> <sup>[18]</sup>	2016	8
19	Kato <i>et al.</i> <sup>[19]</sup>	2014	26
20	Kawahara <i>et al.</i> <sup>[20]</sup>	2011	10
21	Liljenqvist <i>et al.</i> <sup>[21]</sup>	2008	21
22	Luzzati <i>et al.</i> <sup>[22]</sup>	2014	9
23	Matsumoto <i>et al.</i> <sup>[23]</sup>	2013	8
24	Melcher <i>et al.</i> <sup>[24]</sup>	2007	15
25	Sakaura <i>et al.</i> <sup>[25]</sup>	2004	12
26	Salame <i>et al.</i> <sup>[26]</sup>	2015	12
27	Schwab <i>et al.</i> <sup>[27]</sup>	2012	15
28	Shimizu <i>et al.</i> <sup>[28]</sup>	2018	30
29	Sundaresan <i>et al.</i> <sup>[29]</sup>	1989	8
30	Tomita <i>et al.</i> <sup>[30]</sup>	1997	7
31	Tomita <i>et al.</i> <sup>[31]</sup>	1994	20
32	Vasudeva <i>et al.</i> <sup>[32]</sup>	2016	6
33	Wang <i>et al.</i> <sup>[33]</sup>	2018	18
34	Xiao <i>et al.</i> <sup>[34]</sup>	2018	5
35	Xiong <i>et al.</i> <sup>[35]</sup>	2018	5
36	Yang <i>et al.</i> <sup>[36]</sup>	2016	21
37	Yang <i>et al.</i> <sup>[37]</sup>	2016	7
38	Yin <i>et al.</i> <sup>[38]</sup>	2015	26
39	Yokogawa <i>et al.</i> <sup>[39]</sup>	2018	25
40	Yoshioka <i>et al.</i> <sup>[40]</sup>	2013	22
41	Zhong <i>et al.</i> <sup>[41]</sup>	2017	21
42	Zhou <i>et al.</i> <sup>[42]</sup>	2018	12



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