NKR10_Hjernemetastaser_PICO 1

Review information

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What's new

Date / Event	Description

History

Date / Event	Description

Abstract

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Plain language summary

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Background

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Brown 2017

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age (range)*: 61 (54-66) median, IQR ● *No. of metastases*: 77% had 1, 23% had 1-4 ● *Cognitive score (range + scale)*: 72.2 (14.5) baseline, total FACT-Br Control ● *Age (range)*: 62 (54-68) median, IQR ● *No. of metastases*: 74% had 1, 22% had 1-4 ● *Cognitive score (range + scale)*: 71.8 (13.2) baseline, total FACT-Br **Included criteria:** Adult patients (18 years of age or older) with one resected metastatic brain lesion and a resection cavity measuring less than 5·0 cm in maximal extent were eligible for the trial. Up to three unresected metastases (each 3 cm in maximal extent) were allowed. Eligibility criteria included Eastern Cooperative Oncology Group performance status 0–2 and pathology from the resected brain metastasis consistent with a non-CNS primary site. The estimated median overall survival of eligible patients was 9–11 months.1,3,4 The full inclusion and exclusion criteria are given in the protocol (appendix pp 30–122). **Excluded criteria:** Exclusion criteria included pregnant or nursing women, men or women of childbearing potential unwilling to use adequate contraception, inability to complete an MRI scan with contrast, planned chemotherapy during the radiation, previous cranial radiotherapy, leptomeningeal metastases, lesion located within 5 mm of the optic chiasm or within the brainstem, or metastases from primary germ-cell tumours, small-cell carcinoma, or lymphoma. **Pretreatment:** Baseline characteristics were well balanced between the study groups (table 1)
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: stereotactic radiosurgery (SRS) ● *Dosage incl fractions*: For patients randomly assigned to SRS, the prescribed dose was determined by surgical cavity volume: 20 Gy if cavity volume was less than 4·2 mL, 18 Gy if 4·2–7·9 mL, 17 Gy if 8·0–14·3 mL, 15 Gy if 14·4–19·9 mL, 14 Gy if 20·0–29·9 mL, and 12 Gy if 30·0 mL or more up to the maximal surgical cavity extent of 5 cm.8 The surgical cavity was treated with a 2 mm margin. For patients randomly assigned to receive SRS to the surgical cavity, any unresected metastases were treated with SRS with 24 Gy in a single fraction if lesions were less than 1·0 cm, 22 Gy if 1·0–2·0 cm, and 20 Gy if lesions were 2·1–2·9 cm in maximal diameter. ● *Longest follow-up after end of treatment*: Week 12, month 6, 9, 12, 16 and 24 Control ● *Description*: whole brain radiotherapy (WBRT) ● *Dosage incl fractions*: Patients randomly assigned to WBRT were treated with either 30 Gy in ten fractions of 3·0 Gy, or 37·5 Gy in 15 fractions of 2·5 Gy, delivered 5 days a week. Sites predetermined the fractionation schedule, based on institutional preference, that would be used for all patients randomised at the site. For patients randomly assigned to receive WBRT, any unresected metastases were treated with SRS with 22 Gy in a single fraction if lesions were less than 1·0 cm, 20 Gy if 1·0–2·0 cm, and 18 Gy if lesions were 2·1–2·9 cm in maximal diameter.5 For both study groups, the SRS dose was prescribed to the highest isodose line encompassing the target. ● *Longest follow-up after end of treatment*: Week 12, month 6, 9, 12, 16 and 24
Outcomes	*Overall survival, median months (CI)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Notes**: This is overall survival rate from the entire study period. Measured as median. *Overall survival, HR (CI) (lige nu sat som RR)* ● **Outcome type**: DichotomousOutcome *Local recurrence, n Lower is better* ● **Outcome type**: DichotomousOutcome ● **Direction**: Lower is better *Local recurrence, % lower is better* ● **Outcome type**: DichotomousOutcome ● **Direction**: Lower is better *Distant recurrence, n higher is better* ● **Outcome type**: DichotomousOutcome ● **Direction**: Higher is better *Distant recurrence, % higher is better* ● **Outcome type**: DichotomousOutcome ● **Direction**: Higher is better *Neurological impairment, n* ● **Outcome type**: DichotomousOutcome *Cognitive impairment, n* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported

	● **Direction**: Lower is better ● **Data value**: Endpoint ● **Notes**: Measured at 12 months *Decline in quality of life, %* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint ● **Notes**: Obs! Data taken from patients with a decline in life quality at 6 months. Also reported; stable and improvement in life quality. These are not extracted *Local recurrence, n higher is better* ● **Outcome type**: DichotomousOutcome ● **Direction**: Higher is better *Distant reucurrence, n lower is better* ● **Outcome type**: DichotomousOutcome ● **Direction**: Lower is better *Distant reucurrence, %, lower is better* ● **Outcome type**: DichotomousOutcome ● **Direction**: Lower is better *Local recurrence, % higher is better* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Higher is better ● **Data value**: Endpoint ● **Notes**: At 12 months
Identification	**Sponsorship source:** Research reported in this publication was fully supported by the National Cancer Institute of the National Institutes of Health under the Award Numbers U10CA180821 and U10CA180882 (Alliance for Clinical Trials in Oncology NCTN grants), UG1CA189823 (Alliance for Clinical Trials in Oncology NCORP Grant), U10CA011789, U10CA025224, U10CA032291, U10CA076001, U10CA007968, U10CA180790, U10CA180858; and in collaboration with other cooperative groups including Canadian Cancer Trials Group (CCTG) supported by U10CA180863 and CCSRI grant 021039, and NRG Oncology Group, supported by RTOG U10CA21661, NRG U10CA180868, and U10CA180822 from the National Cancer Institute. **Country:** USA **Setting:** 48 institutions in the USA and Canada **Comments:** ClinicalTrials.gov, number NCT01372774 **Authors name:** Paul D Brown **Institution:** Mayo Clinic, Rochester, MN, USA **Email:** brown.paul@mayo.edu **Address:** Department of Radiation Oncology, Mayo Clinic, Rochester, MN 55905, USA
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "We used a dynamic allocation strategy with stratification according to age (<60 years vs ≥ 60 years), duration of extracranial disease control (≤ 3 months vs >3 months), number of brain metastases (one vs two to four), histology (lung vs radioresistant [defined as sarcoma, melanoma, or renal- cell carcinoma] vs other), maximal diameter of the resection cavity (≤ 3 cm vs >3 cm), and treatment centre."
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation group assignment was done electronically via a web-based system. Due to electronic assign ment and the use of a dynamic allocation algorithm, users could not deduce the next assignment in the sequence."
Blinding of participants and personnel (performance bias)	High risk	Quote: "Vol 18 August 2017 1051 Neither patients, clinicians, nor study statisticians were masked to treatment assignment, although the neuro- psychologists grading"
Blinding of outcome assessment (detection bias)	High risk	Quote: "Vol 18 August 2017 1051 Neither patients, clinicians, nor study statisticians were masked to treatment assignment, although the neuro- psychologists grading the cognitive assessments were masked to treatment assignment. Procedures For patients randomly assigned to SRS, the prescribed" Judgement Comment: Unknown if outcome assessors of local and cerebral control where blinded.
Incomplete outcome data (attrition bias)	Low risk	Quote: "Between Nov 10, 2011, and Nov 16, 2015, 194 patients were enrolled and randomly assigned to SRS to the surgical bed (98 patients; five patients did not receive treatment) or WBRT (96 patients; 49 patients received 30 Gy in 10 fractions, 43 received 37·5 Gy in 15 fractions, and four patients did not receive treatment; figure 1). There was one major protocol violation (one patient randomly assigned to the SRS group, whose treatment was switched by the site, received WBRT). Median follow- up was 11·1 months (IQR 5·1–18·0) for all patients and 22·6 months (13·8–34·6) for patients who had not died." Judgement Comment: Missing outcome data seems balanced in numbers across intervention groups (flowchart in figure 1)
Selective reporting (reporting bias)	Low risk	Quote: "This trial is registered with ClinicalTrials.gov, number NCT01372774." Judgement Comment: Protocol marked as study ongoing. Study matches the protocol.
Other bias	Low risk	Quote: "final version of the report. Declaration of interests DR has received honoraria and research support from BrainLab, Varian Medical Systems, Elekta, and Accuray. DK is Senior Vice President and Chief Medical Officer of Varian Medical Systems. The other authors declare no competing interests. Acknowledgments Research reported in this" Quote: "Funding National Cancer Institute." Judgement Comment: The study appears to be free of other sources of bias

Kepka 2016

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age (median, range)*: 59.5 (30-77) ● *No. of metastases*: ● *Cognitive score (range + scale)*: ● *Karnofsky performance score (KPS)*: 83% (KPS 90-100) 17% (KPS 70-80) Control ● *Age (median, range)*: 59.5 (43-78) ● *No. of metastases*: ● *Cognitive score (range + scale)*: ● *Karnofsky performance score (KPS)*: 83% (KPS 90-100). 17% (KPS 70-80) **Included criteria:** Eligibility criteria wereas follows: single brain metastasis found by preoperative MRI ofthe brain, pathologically confirmed metastasis from the solidtumor in the resected brain tumor, total or subtotal resection inthe surgeon's operative report, Karnofsky performance status(KPS)P70, life expectancy > 6 months, no obstacle to performMRI in the follow-up period, and signed informed consent. **Excluded criteria:** Exclusion criteria were as follows: brain metastasis from small-cell lungcancer and hematological malignancies, dementia syndromes, andprevious brain irradiation. **Pretreatment:** Patient characteristics were well balanced in the two treatment-assigned groups as shown inTable 1
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Stereotactic radiotherapy of tumor bed ● *Dosage incl fractions*: SRT-TB was linac based. Patients had post-gadoliniumenhanced T1-weighted MRI (1.5 mm slices) and CT with intra-venous contrast performed for planning. Both sets of images werefused for target delineation. The clinical target volume was definedas the contrast-enhancing surgical cavity with exclusion of the sur-gical tract, postoperative changes and surrounding edema. Con-touring was performed with the aid of a neuro-radiologistwhenever necessary. A three millimeter margin was added to cre-ate the planned target volume. A dose of 15–18 Gy was prescribedat the isodose line (IDL) encompassing the PTV (no lower than 80%IDL, usually 90% IDL). For surgical cavities larger than 5 cm, orthose of irregular complex shape, or in the proximity of criticalstructures for which dose limits with a single fraction would beexceeded, the prescribed dose was 25 Gy given in 5 fractions over5 days. The dose limit for brainstem and chiasma/optic nerves was8 Gy in a single fraction. Patients were immobilized for SRT-TB instereotactic masks system and at the beginning of the study posi-tioned for treatment using a localizing stereotactic frame. During astudy conduction, the conventional frame-based radiosurgery wasreplaced by a frameless image-guided radiosurgery with verifica-tion done by a stereoscopic kilovoltage X-ray system combinedwith infrared position tracking or MV cone beam CT. Radiotherapytechnique consisted of multiple (eight or more) non coplanarmicro-multileaf collimator beams (Brain-LAB, Germany) or volu-metric modulated arc therapy (RapidArcÒ). ● *Longest follow-up after end of treatment*: Week 8, and every 3 months thereafter. Median follow-up was 29 months (range: 8–45) Control ● *Description*: whole-brain radiotherapy ● *Dosage incl fractions*: Patients in the WBRTarm had no MRI done for planning; additionally, CT for planningwas done without intravenous contrast. The WBRT dose was30 Gy in 10 fractions, delivered 5 times weekly at the linear accel-erator. At the beginning of the study treatment plans were dis-cussed with a main study investigator (LK) and a workshop wasorganized for one institution participating in the study. ● *Longest follow-up after end of treatment*: Median follow-up was 29 months (range: 8–45). Median follow-up was 29 months (range: 8–45)
Outcomes	*Overall survival, median months (CI)* ● **Outcome type**: ContinuousOutcome *Overall survival, HR (CI) (lige nu sat som RR)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Partially reported ● **Direction**: Lower is better ● **Notes**: Hazard ratio for SRT group reported. Hazard ratio manually set to 1.0 in the WBRT group. *Local recurrence, n Lower is better* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Notes**: Relapse in tumor bed within 2 years *Local recurrence, % lower is better* ● **Outcome type**: DichotomousOutcome *Distant recurrence, n higher is better* ● **Outcome type**: DichotomousOutcome *Distant recurrence, % higher is better* ● **Outcome type**: DichotomousOutcome *Neurological impairment, n* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Notes**: Neurological impairment with and without progression in the brain *Cognitive impairment, n*

	● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Notes**: Neurological impairment with and without progression in the brain *Decline in quality of life, % Obs! 6 mdr* ● **Outcome type**: DichotomousOutcome *Local recurrence, n higher is better* ● **Outcome type**: DichotomousOutcome *Distant reucurrence, n lower is better* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Notes**: Progression at new sites. Overall within 2 years. *Distant reucurrence, %, lower is better* ● **Outcome type**: DichotomousOutcome *Local recurrence, % higher is better* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** All authors declare no conflict of interest.There was no founding source for this study. **Country:** Poland **Comments:** The study was registered with Clini-calTrails.gov under number NCT0153520 **Authors name:** Lucyna Kepka **Institution:** Head of Radiation Oncology Department, IndependentPublic Health Care Facility of the Ministry of the Interior, and Warmian Masurian Oncology Centre **Email:** lucynak@coi.pl **Address:** Head of Radiation Oncology Department, IndependentPublic Health Care Facility of the Ministry of the Interior, and Warmian MasurianOncology Centre, Al. Wojska Polskiego 37, 10-228 Olsztyn, Poland.
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization based on the minimization method was per- formed by telephone to a central datacenter."
Allocation concealment (selection bias)	Low risk	Quote: "Randomization based on the minimization method was per- formed by telephone to a central datacenter."
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Insufficient information on blinding of paticipants and personnel
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Insufficient information on blinding of outcome assesors
Incomplete outcome data (attrition bias)	Low risk	Quote: "Fifteen patients were alive (5 in the SRT-TB arm and 10 in the WBRT arm) at the time of analysis; the median follow-up being 29 months (range: 8–45). None of the patients were lost to follow-up regarding vital status. Two-year OS rates (in the intention-to-treat analysis) were 10% (95% confidence interval [CI]: 0–22%) in the SRT-TB arm and 37% (95% CI:19–55%) in the WBRT arm, p = 0.046; hazard ratio (HR) was 1.8 (95% CI: 0.99– 3.30) (Fig. 2). Two-year CIND rates were 66% (95% CI: 46–86%) and 31% (95% CI: 14–49%) in SRT-TB and WBRT arms, respectively, p = 0.015; HR was 2.51 (95% CI: 1.19–5.29) (Fig. 3)." Judgement Comment: Missing data balanced across intervention groups (1 excluded in SRT-TB group and none in the WBRT group)
Selective reporting (reporting bias)	Low risk	Quote: "The protocol was approved by the ethics committees from the participating institutions. The study was registered with Clini- calTrails.gov under number NCT01535209 and was conducted according to the Declaration of Helsinki."
Other bias	Low risk	Quote: "more evidence in this field. Declaration of interest All authors declare no conflict of interest. There was no founding source for this study. References [1] Patchell R, Tibbs"

Kepka 2017

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Included criteria:** Briefly, entry criteria included single brainmetastasis found by preoperative MRI of the brain, pathologically confirmed metastasis from the solid tumorin the resected brain metastasis, total or subtotal resectionin the surgeon's operative report, Karnofsky performancestatus (KPS)C70, life expectancy[6 months, and noobstacle to perform MRI in the follow-up period **Excluded criteria:** See Kepka 2016 **Pretreatment:** See Kepka 2016
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Stereotactic radiotherapy of tumor bed ● *Dosage incl fractions*: RT-TB was given at the single dose of 15–18 or 25 Gyin five fractions for large- or irregular-shaped surgicalcavities. Patients had post-gadolinium-enhanced T1-weighted MRI (1.5-mm slices) and CT with intravenouscontrast performed for planning. The clinical target volumewas defined as the contrast-enhancing surgical cavity withexclusion of the surgical tract. A 3-mm margin was addedto create the planned target volume. ● *Longest follow-up after end of treatment*: 5 months after RT Control ● *Description*: Whole brain radiation ● *Dosage incl fractions*: Patients in the WBRTarm had no MRI performed for planning. The WBRT dosewas 30 Gy in

	ten fractions, delivered five times weekly atthe linear accelerato ● *Longest follow-up after end of treatment*: 5 months after RT
Outcomes	*Overall survival, median months (CI)* ● **Outcome type**: ContinuousOutcome *Overall survival, HR (CI) (lige nu sat som RR)* ● **Outcome type**: DichotomousOutcome *Local recurrence, n Lower is better* ● **Outcome type**: DichotomousOutcome *Local recurrence, % lower is better* ● **Outcome type**: DichotomousOutcome *Distant recurrence, n higher is better* ● **Outcome type**: DichotomousOutcome *Distant recurrence, % higher is better* ● **Outcome type**: DichotomousOutcome *Neurological impairment, n* ● **Outcome type**: DichotomousOutcome *Cognitive impairment, n* ● **Outcome type**: DichotomousOutcome *Decline in quality of life, %, change, 6 mdr* ● **Outcome type**: DichotomousOutcome *Local recurrence, n higher is better* ● **Outcome type**: DichotomousOutcome *Distant reucurrence, n lower is better* ● **Outcome type**: DichotomousOutcome *Distant reucurrence, %, lower is better* ● **Outcome type**: DichotomousOutcome *Local recurrence, % higher is better* ● **Outcome type**: DichotomousOutcome *Quality of life, end of treatment (SD), 5 months* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: QoL-BN20 (subscale functional uncertainty) ● **Direction**: Lower is better ● **Data value**: Endpoint ● **Notes**: QoL-BN20 (subscale functional uncertainty), Mean (SD). End of treatment. At 5 months
Identification	**Sponsorship source:** The authors report no conflict of interest. **Country:** Poland **Comments:** NCT01535209 **Authors name:** L. Kepka **Institution:** Military Institute of Medicine **Email:** lkepka@wim.mil.pl **Address:** Ul. Szasero´w 128,04-141 Warsaw, Poland
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement Comment: Randomization based on the minimization method was performedby telephone to a central datacenter. Patients were strati-fied according to the institution, the presence of extracranialdisease, KPS (100–90 versus 80–70), and so called ‘‘radioresistant”histology (melanoma or renal cancer) versus others. (se artiklel 2016) Details taken from Kepka et al 2016. Randomization was done my minimization method, performed by telephone to a central datacenter.
Allocation concealment (selection bias)	Low risk	Judgement Comment: Taken from Kepka et al 2016. Randomization was done by minimization method, performed by telephone to a central datacenter.
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Nothing mentioned
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Nothing mentioned
Incomplete outcome data (attrition bias)	Unclear risk	Quote: "Compliance with HRQOL measures dropped to 52% [30 patients: 12 (50%) of those receiving SRT-TB and 18 (53%) of those receiving WBRT] at 5 months. We received only 16 (28%) filled QLQ-C30 and QLQ-BN20 question- naires at 8 months. Thus, with such low compliance we decided to stop our analysis of HRQOL at 5 months of follow-up." Judgement Comment: No ITT
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: Secondary outcome: Quality of life assessment [Time Frame: 2 years]Trial registration: NCT01535209 The study was stopped at 5 months due to low compliance.
Other bias	Low risk	Quote: "Conflict of interest The authors report no conflict of interest."

Kerschbaumer 2016

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	
Interventions	
Outcomes	*Overall survival, median months (CI)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Partially reported ● **Direction**: Higher is better ● **Notes**: Reported as median. No variance. *Overall survival, HR (CI) (lige nu sat som RR)* ● **Outcome type**: DichotomousOutcome *Local recurrence, n Lower is better* ● **Outcome type**: DichotomousOutcome ● **Direction**: Lower is better ● **Notes**: Local recurrence in the control group occured within 3 months. *Local recurrence, % lower is better* ● **Outcome type**: DichotomousOutcome *Distant recurrence, n higher is better* ● **Outcome type**: DichotomousOutcome *Distant recurrence, % higher is better* ● **Outcome type**: DichotomousOutcome *Neurological impairment, n* ● **Outcome type**: DichotomousOutcome *Cognitive impairment, n* ● **Outcome type**: DichotomousOutcome *Decline in quality of life, % Obs! 6 mdr* ● **Outcome type**: DichotomousOutcome *Local recurrence, n higher is better* ● **Outcome type**: DichotomousOutcome *Distant reucurrence, n lower is better* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Notes**: A distant progression was noted in 3 patients after WBRT within 9 (3-20) months and 4 patients after SI developed dis-tant metastases after a mean of 5 (1-9) months (n.s.). *Distant reucurrence, %, lower is better* ● **Outcome type**: DichotomousOutcome *Local recurrence, % higher is better* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** Not reported **Country:** Austria **Authors name:** Johannes Kerschbaumer **Institution:** Department of Neurosurgery, Medical University of Innsbruck, Innsbruck, Austria, **Email:** not reported **Address:** Department of Neurosurgery, Medical University of Innsbruck, Innsbruck, Austria,
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "study is a monocentric, randomized trial in patients with a singular brain metastasis." Judgement Comment: Insufficient information on sequence generation
Allocation concealment (selection bias)	High risk	Quote: "the tumor bed and a surrounding 6 mm security margin. METHODS: The study is a monocentric, randomized trial in patients with a singular brain metastasis. Efficacy was" Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Insufficient information on blinding of participants
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias)	Unclear risk	Judgement Comment: Insufficient information on the group distribution of inclomplete outcome data Only abstract available.
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: No reference to study protocol
Other bias	Unclear risk	Judgement Comment: Insufficient information on conflict of interest or funding source

Footnotes

Characteristics of excluded studies

Baker 2016

Reason for exclusion	Wrong study design

Bernhardt 2017

Reason for exclusion	Wrong study design

Dhakal 2014

Reason for exclusion	Wrong study design

Eichorn 2016

Reason for exclusion	Wrong study design

Flores 2016

Reason for exclusion	Wrong study design

Fogarty 2016

Reason for exclusion	Wrong comparator

Fuchs 2017

Reason for exclusion	Wrong study design

Igaki 2017

Reason for exclusion	Wrong study design

Iorio Morin 2014

Reason for exclusion	Wrong study design

Kayama 2016

Reason for exclusion	Wrong comparator

Kepka 2016a

Reason for exclusion	Abstract of an already included article

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

References to studies

Included studies

Brown 2017

Brown, Paul D.; Ballman, Karla V.; Cerhan, Jane H.; Anderson, S. K.; Carrero, Xiomara W.; Whitton, Anthony C.; Greenspoon, Jeffrey; Parney, Ian F.; Laack, Nadia N. I.; Ashman, Jonathan B.; Bahary, Jean-Paul; Hadjipanayis, Costas G.; Urbanic, James J.; Barker, Fred G.,2nd; Farace, Elana; Khuntia, Deepak; Giannini, Caterina; Buckner, Jan C.; Galanis, Evanthia; Roberge, David. Postoperative stereotactic radiosurgery compared with whole brain radiotherapy for resected metastatic brain disease (NCCTG N107C/CEC.3): a multicentre, randomised, controlled, phase 3 trial. The Lancet.Oncology 2017;18(8):1049-1060. [DOI: https://dx.doi.org/10.1016/S1470-2045(17)30441-2]

Kepka 2016

Kepka, Lucyna; Tyc-Szczepaniak, Dobromira; Bujko, Krzysztof; Olszyna-Serementa, Marta; Michalski, Wojciech; Sprawka, Arkadiusz; Trabska-Kluch, Berenika; Komosinska, Katarzyna; Wasilewska-Tesluk, Ewa; Czeremszynska, Beata. Stereotactic radiotherapy of the tumor bed compared to whole brain radiotherapy after surgery of single brain metastasis: Results from a randomized trial. Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology 2016;121(2):217-224. [DOI: https://dx.doi.org/10.1016/j.radonc.2016.10.005]

Kepka 2017

Kepka L.; Tyc-Szczepaniak D.; Osowiecka K.; Sprawka A.; Trabska-Kluch B.; Czeremszynska B.; Olszyna-Serementa M.. Quality of life: Result from a randomized trial that compared WBRT with radiosurgery of tumor cavity. Radiotherapy and Oncology 2017;123(Journal Article):S327-S328. [DOI:]

Kerschbaumer 2016

Kerschbaumer J.; Pinggera D.; Seiz-Rosenhagen M.; Nevinny-Stickel M.; Thome C.; Freyschlag C.. Sector irradiation vs. Whole-brain irradiation after resection of singular brain metastasis-interim analysis of a prospective randomized monocentric trial. Neuro-oncology 2016;18(Journal Article). [DOI: http://dx.doi.org/10.1093/neuonc/now212.125]

Excluded studies

Baker 2016

Baker S.; Lim G.; Nordal R.; Surgeoner B.; Kostaras X.; Roa W.. Provincial clinical practice guidelines for patients with 1-3 brain metastases. Radiotherapy and Oncology 2016;120(Journal Article):S77. [DOI:]

Bernhardt 2017

Bernhardt D.; Adeberg S.; Bozorgmehr F.; Kappes J.; Hoerner-Rieber J.; Koenig L.; Debus J.; Thomas M.; Unterberg A.; Herth F.; Heussel C.P.; Steins M.; Rieken S.. Outcomes and prognostic factors in solitary brain metastasis from small cell lung cancer. Radiotherapy and Oncology 2017;123(Journal Article):S652-S653. [DOI:]

Dhakal 2014

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Eichorn 2016

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Studies awaiting classification

Ongoing studies

Other references

Additional references

Other published versions of this review

Classification pending references

Data and analyses

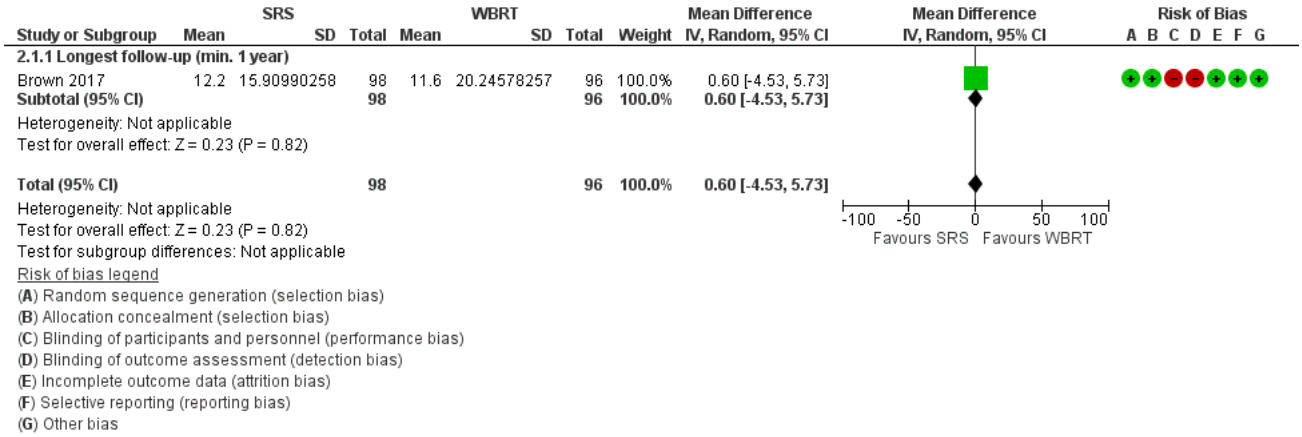
2 SRS vs WBRT

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 Overall survival, median months (CI)	1	194	Mean Difference (IV, Random, 95% CI)	0.60 [-4.53, 5.73]
2.1.1 Longest follow-up (min. 1 year)	1	194	Mean Difference (IV, Random, 95% CI)	0.60 [-4.53, 5.73]
2.2 Quality of life, end of treatment (SD), 5 months	1	30	Mean Difference (IV, Fixed, 95% CI)	-11.40 [-30.15, 7.35]
2.2.1 Longest follow-up (min. 1 year)	1	30	Mean Difference (IV, Fixed, 95% CI)	-11.40 [-30.15, 7.35]

2.3 Overall survival 2 years	1		Hazard Ratio (IV, Fixed, 95% CI)	1.80 [0.99, 3.27]
2.6 Local control, n (Event = local control)	2	241	Risk Ratio (IV, Random, 95% CI)	0.81 [0.59, 1.10]
2.6.1 Longest follow-up (min 1 year)	2	241	Risk Ratio (IV, Random, 95% CI)	0.81 [0.59, 1.10]
2.8 Distant control, n (Event = local control)	2	241	Risk Ratio (IV, Random, 95% CI)	0.73 [0.62, 0.85]
2.8.1 Longest follow-up (min 1 year)	2	241	Risk Ratio (IV, Random, 95% CI)	0.73 [0.62, 0.85]
2.11 Neurological impairment, n	1	40	Risk Ratio (IV, Fixed, 95% CI)	0.63 [0.35, 1.12]
2.11.1 Longest follow-up (min. 1 year)	1	40	Risk Ratio (IV, Fixed, 95% CI)	0.63 [0.35, 1.12]
2.12 Cognitive impairment, n	2	88	Risk Ratio (IV, Random, 95% CI)	0.65 [0.46, 0.92]
2.12.1 Longest follow-up (min 1 year)	2	88	Risk Ratio (IV, Random, 95% CI)	0.65 [0.46, 0.92]
2.14 Decline in quality of life, n 6 months	1	129	Risk Ratio (IV, Fixed, 95% CI)	0.62 [0.36, 1.06]
2.14.1 Longest follow-up (min. 1 year)	1	129	Risk Ratio (IV, Fixed, 95% CI)	0.62 [0.36, 1.06]

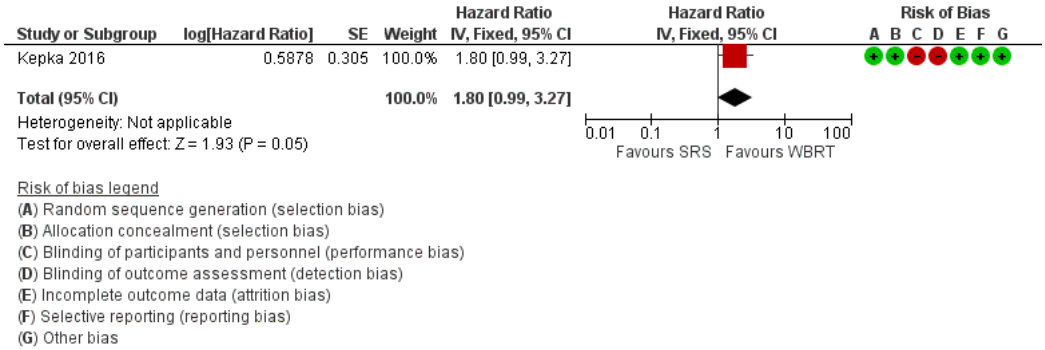
Figures

Figure 1 (Analysis 2.1)



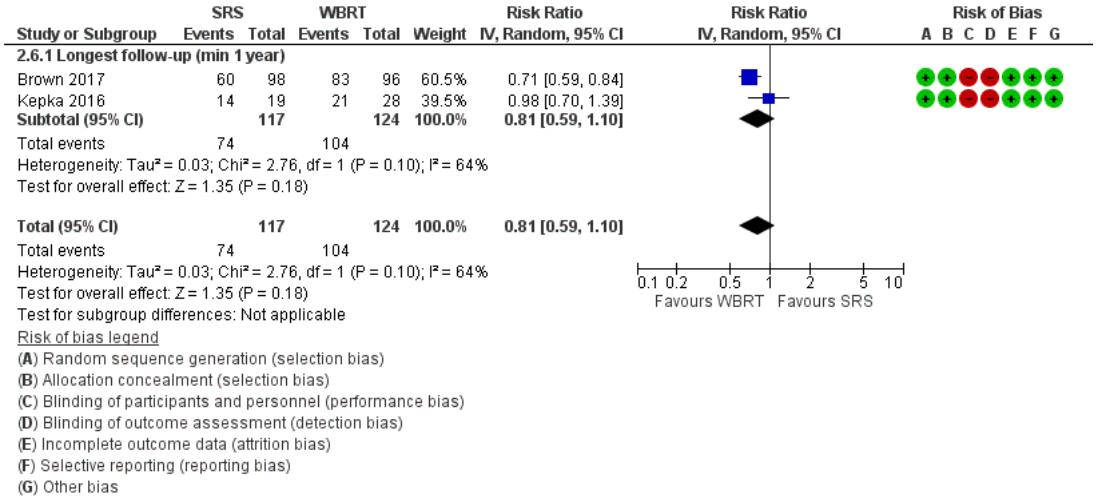
Forest plot of comparison: 2 SRS vs WBRT, outcome: 2.1 Overall survival, median months (CI).

Figure 2 (Analysis 2.3)



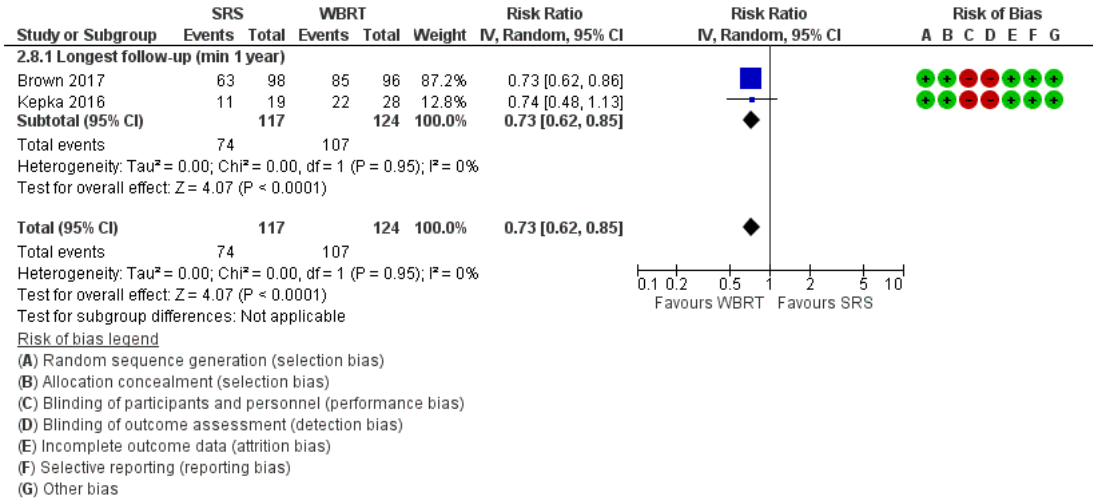
Forest plot of comparison: 2 SRS vs WBRT, outcome: 2.3 Overall survival 2 years.

Figure 3 (Analysis 2.6)



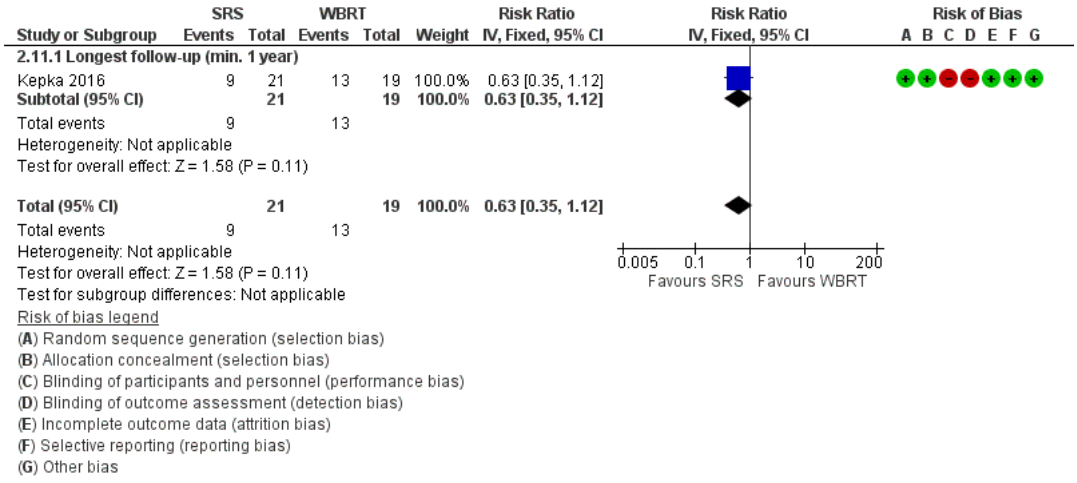
Forest plot of comparison: 2 SRS vs WBRT, outcome: 2.6 Local control, n (Event = local control).

Figure 4 (Analysis 2.8)



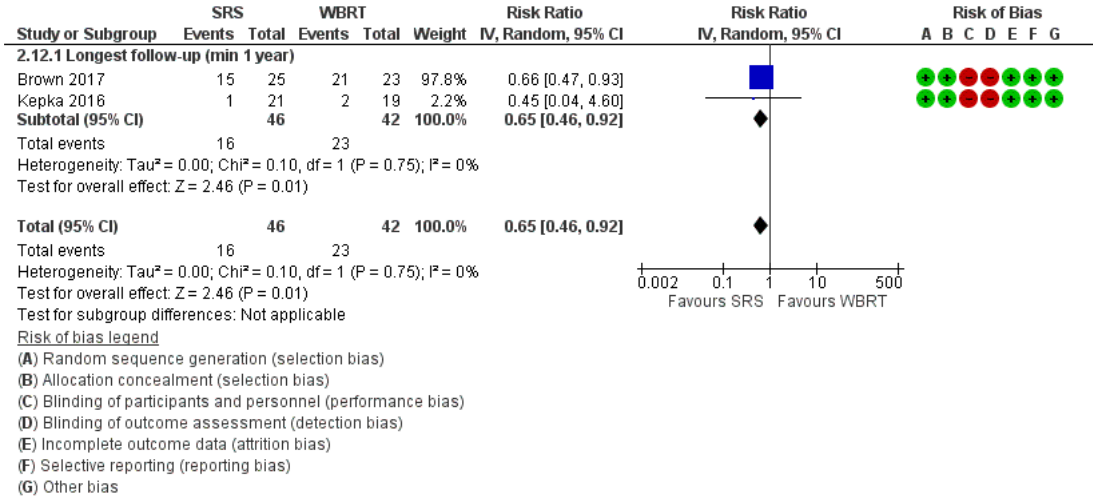
Forest plot of comparison: 2 SRS vs WBRT, outcome: 2.8 Distant control, n (Event = local control).

Figure 5 (Analysis 2.11)



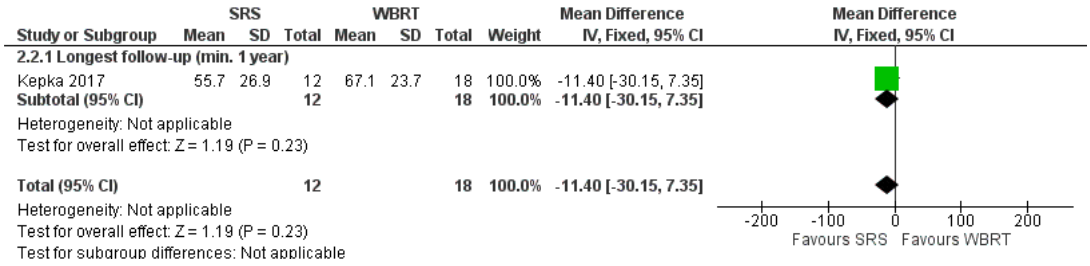
Forest plot of comparison: 2 SRS vs WBRT, outcome: 2.11 Neurological impairment, n.

Figure 6 (Analysis 2.12)



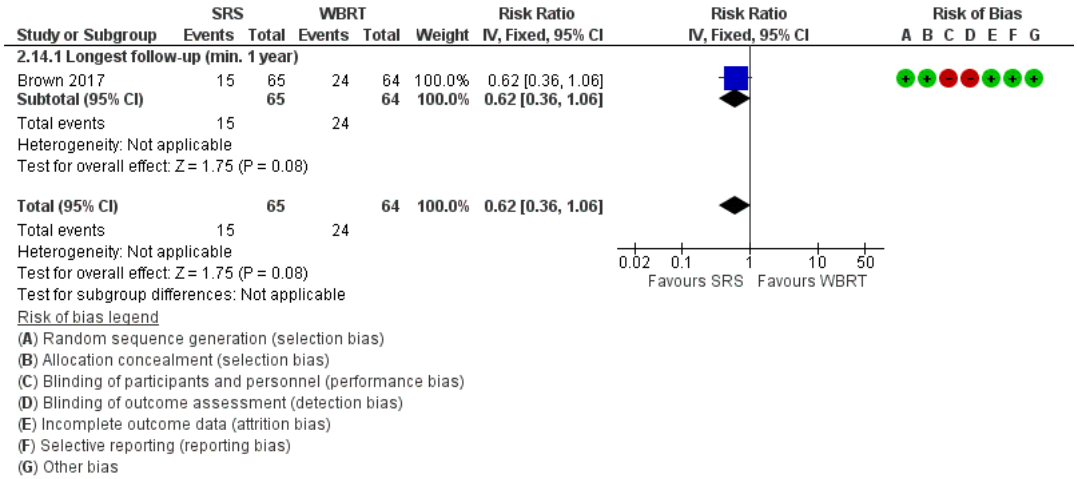
Forest plot of comparison: 2 SRS vs WBRT, outcome: 2.12 Cognitive impairment, n.

Figure 7 (Analysis 2.2)



Forest plot of comparison: 2 SRS vs WBRT, outcome: 2.2 Quality of life, end of treatment (SD), 5 months.

Figure 8 (Analysis 2.14)



Forest plot of comparison: 2 SRS vs WBRT, outcome: 2.14 Decline in quality of life, n 6 months.

Sources of support

Internal sources

- No sources of support provided

External sources

- No sources of support provided

Feedback

Appendices