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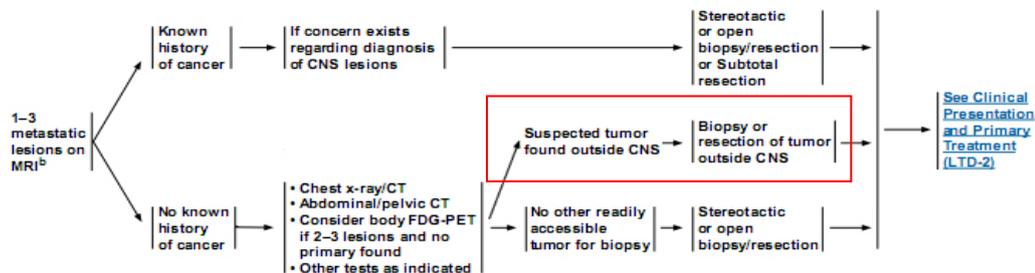
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Date of request: 2015.08.23

NCCN Guidelines Panel:

I respectfully request the NCCN (NCCN guidelines version 1.2015 Central Nervous System Cancers) to review the the following inappropriate statements about brain metastatic lesions.

1. In LTD-1, the content in the red text box should be located at the current position.



²See Principles of Brain Tumor Imaging (BRAIN-A).

³Consider a multidisciplinary review in treatment planning, especially once pathology is available (See Principles of Brain Tumor Management (BRAIN-E)).

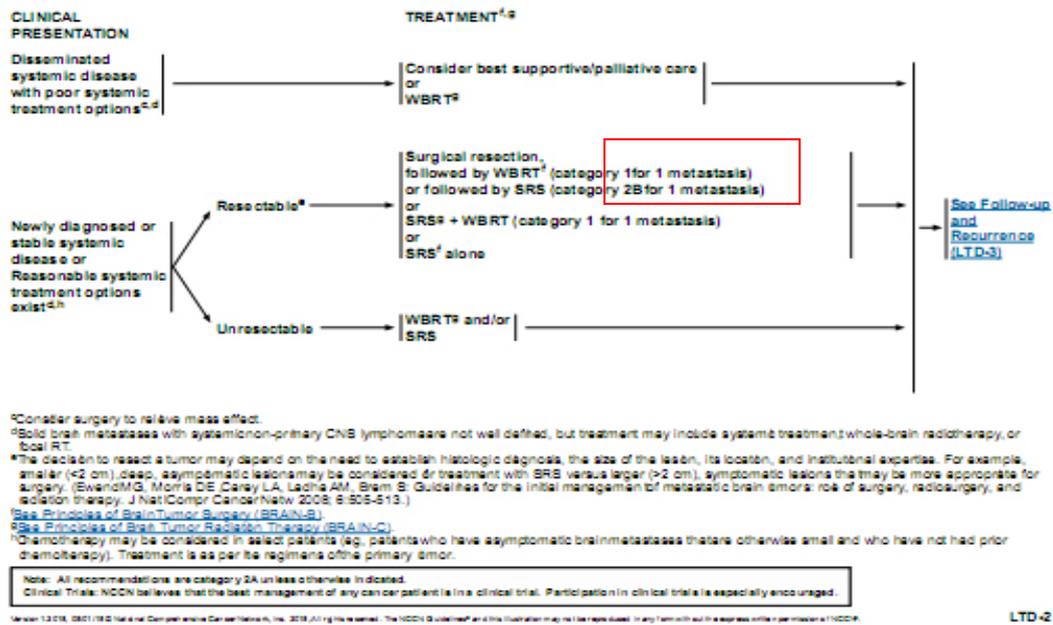
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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LTD-1

Rationale: Patients with 1-3 metastatic lesions on MRI, who have no known cancer history, require a careful systemic workup. If suspected tumor is found outside CNS, a biopsy or resection is needed.

2. In LTD-2, “for 1 metastasis” should be emphasized(as shown in red text box).



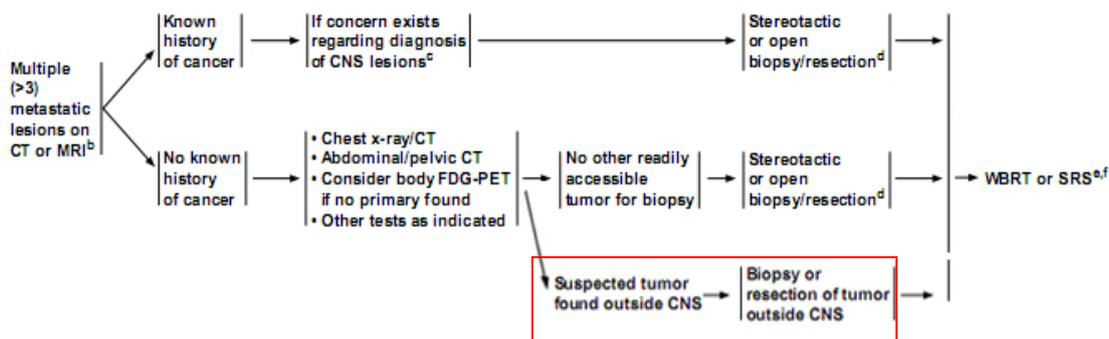
Rationale: The evidence of surgical resection followed by WBRT is two RCTs: one from Patchell RA(1998) and the other is EORTC 22952-26001 Study. In Patchell RA’ study, Ninety-five patients who had **single** metastasis to the brain that were treated with complete surgical resections (as verified by postoperative magnetic resonance imaging) between September 1989 and November 1997 were entered into the study. In EORTC 22952-26001 Study, patients with single metastatic lesion accounted for **94%** in S/Observation group, and **98%** in S/WBRT group. There were no patients with 3 metastatic lesions in both groups. So the evidence of surgical resection followed by WBRT is mainly about patients with single metastatic lesion.

The evidence of surgical resection + SRS is also mainly about patients with single metastatic lesion(as following, no RCTs evidence). But how can we draw the conclusion about patients with 1-3 metastatic lesions.

author(year)	No. of Patients (No. of lesions)	Size (cc)	1y OS (%)	1y LC (%)
Soltys (2008)	72 (76)	9.8(0.1-66.8)	57	79
Karlovits (2009)	52 (61)	3.85(0.08-22)		
Kelly (2012)	17 (18)	3.49 (0.53-10.8)	93	89
Choi (2012)	112 (120)	8.5 (0.08-66.8)	62	90.5
Hartford (2013)	47 (49)	11.5 (1.1-36)	52.5	85.5

Minniti (2013)	101(101)	17.5(12.6-35.7)	69	93
Ling (2015)	99 (100)	>3cm	55	72

3. In MU-1, the content in the red text box should be added to the current position.



^aSee Principles of Brain Tumor Imaging (BRAIN-A).

^bConsider a multidisciplinary review in treatment planning, especially once pathology is available (See Principles of Brain Tumor Management (BRAIN-E)).

^cAs part of diagnostic evaluation, neuroimaging modalities such as MRI, DW-MRI, MRI-SPECT, or PET scan may be considered.

^dConsider surgery to relieve mass effect.

^eSee Principles of Brain Tumor Radiation Therapy (BRAIN-C).

^fSRS can be considered for patients with good performance and low overall tumor volume. (Chang WS, Kim HY, Chang JW, et al. Analysis of radiosurgical results in patients with brain metastases according to the number of brain lesions: is stereotactic radiosurgery effective for multiple brain metastases? J Neurosurg 2010;113 Suppl:73-78).

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See Follow-up and Recurrence (MU-2)

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MU-1

Rationale: “no meat, no treat”, I think it is a error of omission.

4. In the last paragraph of MS-26, the statements of “However, many patients are not candidates of resection because of the inaccessibility of the tumor, extensive systemic disease, or other factors. WBRT is the main choice of primary therapy for this patient group.” may be corrected as “WBRT or SRS or both together is the main choice of primary therapy for this patient group.”

Rationale: SRS but not WBRT is suitable for the patients with inaccessible tumor or poor performance status because of comorbidities.

5. The citation of Ref. 271 is not appropriate.

Rationale: The conclusion is about SRS+WBRT vs SR+WBRT. However, the evidence(Ref. 271) is about SRS vs SR. The title of the paper is “A COMPARISON OF SURGICAL RESECTION AND STEREOTACTIC RADIOSURGERY IN THE TREATMENT OF SOLITARY BRAIN METASTASES” and the statements in the paper is “There were no significant differences between 74 NS and 23 RS patients in terms of baseline characteristics (age, gender, systemic disease type, systemic disease status, signs/symptoms at SBM presentation) or percent of patients who received whole brain radiotherapy.” Here, whole brain radiotherapy is a balanced

confounding variable.

I would be greatly appreciated if you could spend some of your time on checking my suggestions.

Looking forward to hearing from you.

Thank you and best regards.

Yours sincerely