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NCCN Guidelines Panel: Non-Small Cell Lung Cancer

The Society of Interventional Oncology (SIO) is a non-profit association that supports and promotes the field of interventional oncology (IO) through professional development, access advocacy and research, and physician community building. SIO's mission is to advance interventional oncology by developing evidence supporting IO treatments, educating IO practitioners, and improving patient access to IO procedures. SIO provides support for the worldwide community of IO practitioners with a mission to advance minimally invasive oncologic therapies that harmonize with medical oncology, surgical oncology, radiation oncology, and palliative medicine.

On behalf of the Society of Interventional Oncology, we respectfully request the NCCN Non-Small Cell Lung Cancer (NSCLC) guideline panel review the enclosed data and consider updating the role of image-guided thermal ablation (IGTA) in the Clinical Practice Guidelines in Oncology (NCCN Guidelines) for NSCLC.

IGTA comprises radiofrequency ablation, microwave ablation, and cryoablation. IGTA is currently included in the NSCLC Clinical Practice Guidelines primarily as a therapeutic modality among “high risk” patients. However, **an abundance of data suggest IGTA is safe and efficacious in a variety of clinical settings, including studies suggesting similar outcomes to radiotherapy and surgical resection in selected patients.** We believe the Specific Changes delineated below reflect the best data currently available for review on IGTA.

Specific Change 1: On NSCL-2, for Stage IA Medically inoperable, remove footnote “m” and include “Image-guided thermal ablation” in the main treatment algorithm below “Definitive RT including stereotactic ablative radiotherapy”

Rationale: A large body of evidence demonstrates the safety and long-term efficacy of IGTA when used for local control among patients with stage IA non-small cell lung cancer. Nearly twenty years of data support this approach, including multiple prospective clinical trials. In the multicenter RAPTURE trial of IGTA, for example, a complete response rate of 88% was achieved at one year among patients with early-stage lung cancers with a one-year cancer-specific survival of 92% (Lencioni et al. 2008). In the subsequent prospective multicenter Alliance trial of patients with stage IA lung cancer, overall survival was 86.3% at one year (Dupuy et al. 2015). No grade 4 or 5 adverse events were attributable to IGTA, and there was no observed change in FEV1 or DLCO. Similar results were obtained by Ambroggi et al. (2011), who demonstrated a median overall survival of 33.4 months and cancer-specific survival of 41.4 months following IGTA for stage I lung cancer, and Palussiere et al. (2018), who achieved 84% one-year recurrence free survival and 91.7% one-year overall survival with IGTA for stage IA lung cancer.

More recently, a propensity score-matched National Cancer Database study (Uhlig et al. 2021) demonstrated no significant difference in overall survival following IGTA when compared with stereotactic body radiotherapy (SBRT) for treatment of stage I NSCLC. A separate study comparing IGTA and SBRT outcomes using the Surveillance, Epidemiology, and End Results (SEER) Database found similar five-year overall survival between modalities (Li et al. 2021). A recent systematic review and meta-analysis found similar overall and progression-free survival as well as local progression when compared with SBRT (Chen et al. 2022).

Finally, a recent multicenter cohort analysis demonstrated a median overall survival of 64.2 months when microwave ablation was in stage I NSCLC patients (Ni et al. 2022). These and other data support the inclusion of IGTA within the main treatment algorithm alongside radiation therapy for medically inoperable patients with NSCLC.

Specific Change 2: On NSCL-15, Definitive therapy for local disease feasible → T1-3, N0, change “Surgical resection or SABR” to “Surgical resection, SABR or IGTA”.

Rationale: A continually growing volume of literature demonstrates the long-term efficacy of IGTA for local control of primary lung cancer. IGTA may be of particular value in patients with limited pulmonary reserve or those who have reached the limits of tissue toxicity from radiation therapy with similar oncologic outcomes. For example, in a 2018 National Cancer Database study comparing IGTA and stereotactic radiation therapy for treatment of stage I lung cancer, no significant difference in overall survival was identified between modalities after a mean follow-up duration of 52.4 months (Uhlir et al. 2018). In a separate comparing IGTA and stereotactic radiation therapy for treatment of early-stage lung cancer, no difference in 1-, 3-, or 5-year overall survival rates were observed between groups (Lam et al. 2018). In a comparative study of IGTA, stereotactic radiation, and sublobar lung resection by Iguchi et al. (2020), no significant difference in overall or progression-free survival was identified between ablation and radiation at 5 years. In a 2020 study by Zeng et al. using data from the Surveillance, Epidemiology, and End Results (SEER) database, IGTA demonstrated a 5-year overall survival rate of 47.8%, similar to wedge resection for patients older than 75 years of age. Similarly, in a recent systematic review and meta-analysis of patients treated with IGTA or surgical resection for stage I NSCLC, no differences in overall or disease-free survival were noted at one and three years (Chan et al. 2021). These and other data support the inclusion of IGTA alongside surgery and radiation as a therapeutic option when definitive therapy for local disease is feasible.

Specific Change 3: On NSCL-15, change footnote “hh” to read “Typically, RT (including SABR), IGTA, or surgical resection”.

Rationale: IGTA is a safe and effective therapeutic option for patients with metastatic NSCLC in whom definitive local therapy is feasible. IGTA as a modality is associated with low morbidity, low mortality, and can be repeated multiple times without accrual of excess toxicity. There is demonstrated efficacy of this approach using IGTA. The prospective multicenter SOLSTICE study of IGTA for lung metastases (Callstrom et al. 2020) demonstrated a local control rate of 85.1% at one year with a two-year overall survival rate of 86.6%. In this study, the grade IV toxicity rate was 0.6%, and no clinically relevant decrement in performance status or healthcare-related quality of life were observed at two years of follow up. Based on these data, IGTA should be formally included as a safe and effective therapeutic modality that may expand the pool of patients in whom a local consolidative therapy approach to limited metastatic disease is feasible.

Specific Change 4: On NSCL-17, for “Resectable recurrence” of “Locoregional recurrence or symptomatic local disease,” remove footnote “n” and move “IGTA” to the main treatment algorithm under “External-beam RT or SABR”.

Rationale: Due to the low morbidity and lack of significant cumulative toxicity to pulmonary parenchyma and environs, IGTA should be included alongside radiation therapy as an option for NSCLC patients with locoregional recurrence. In recent publications, IGTA has been shown to demonstrate similar long-term outcomes when compared with radiation therapy, as described in detail above (See: *Specific Change 1 & 2*). IGTA can be employed in a single treatment session, even among patients who have previously undergone surgical resection, have previously received radiation therapy, and/or those patients with limited baseline pulmonary reserve who desire local treatment. IGTA can also be repeated, where necessary.

Specific Change 5: On NSCL-21, 22, 24 and 25, change each instance of “Consider definitive local therapy (eg, SABR or surgery) for limited lesions to “Consider definitive local therapy (eg, IGTA, SABR or surgery) for limited lesions.”

Rationale: IGTA can be safely employed as a curative-intent therapy alone or in combination with systemic therapies including tyrosine kinase inhibitors. For example, in a meta-analysis of tyrosine kinase inhibitors targeting epidermal growth factor receptor (EGFR), showed significantly increased rates of complete response and disease control when IGTA was added to EGFR therapy when compared with EGFR therapy alone among patients with non-small cell lung cancer (Li et al. 2021). Similarly, in a cohort study by Yu et al. (2013), the application of local therapy (including IGTA) alongside continued EGFR targeted therapy for patients with advanced lung cancer was safe and effective, with median time to progression of 10 months, median time to a change in systemic therapy of 22 months, and median overall survival following local therapy of 41 months. These data support the inclusion of IGTA into the formal treatment algorithm when pursuing definitive local therapy for local lesions in the context of EGFR mutant lung cancers receiving targeted systemic therapies.

Specific Change 6: In “Discussion: Treatment Approaches”, add a section titled “Image-Guided Thermal Ablation” following MS-32 “Whole Brain RT and Stereotactic Radiosurgery” but preceding MS-33 “Combined Modality Therapy.”

Rationale: Image-guided thermal ablation is widely utilized in clinical practice among patients with non-small cell lung cancer, including as primary therapy for solitary and multifocal primary lung cancer as well as for treatment of recurrent and oligometastatic disease. A discussion that summarizes the existing literature and highlights these potential applications of IGTA would be a useful to include as a reference for lung cancer practitioners under “Discussion: Treatment Approaches.”

Sincerely,

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