Image-guided Tumor Ablation:

Proposal for Standardization of Terminology and Reporting Criteria

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Introduction:

For the past four years, the International Working Group on Image-guided Tumor Ablation has been meeting informally at the Radiologic Society of North America (RSNA) annual meeting to discuss and gain a better understanding of the many new techniques and technologies that are currently available, or that are being studied for potential use as minimally invasive cancer treatments. The venue of the RSNA has permitted a wide international representation of investigators, including those with extensive experience in the development and use of many of the thermal and chemical therapies available for the treatment of liver and other focal malignancies. Through our discussions over the years, it was acknowledged that this new field of image-guided tumor ablation required standardization of terminology and reporting criteria to facilitate effective communication of ideas and appropriate comparison between treatments that use different technologies. Based upon this insight, a working committee was established and charged with the goal of producing a position paper on such standardization. This committee was selected to have wide geographic representation and expertise in all areas of image-guided tumor ablation. The position paper was unanimously adopted by the committee and has been ratified by the International Working Group on Image-guided Tumor Ablation members found in the appendix. It is therefore our hope and intention that adherence to the recommendations of this position paper will facilitate achieving our main objectives -- improved precision and communication in this field leading to more accurate comparison of technologies, results, and ultimately to improved patient outcomes.

A. Classification of Therapies:

Image-guided Tumor Ablation: The term "**tumor ablation**" is defined as the direct application of chemical or thermal therapies to a specific focal tumor (or tumors) in an attempt to achieve eradication or substantial tumor destruction [1 - 6]. The term "direct" aims to distinguish these therapies from those that are applied orally or via an intravascular or peripheral venous route. We stress the concept of image guidance in the title of our field given our radiologic perspective and to highlight that image guidance is critical to the success of these therapies [1 - 6]. Given that most of these therapies can be performed using a host of imaging modalities (i.e., ultrasound, CT, MR, and fluoroscopy), the more general term of "**image-guidance**" is preferred, unless a particular imaging modality is mandated as part of the technique. However, virtually all available ablation techniques can theoretically be used with all modalities.

While previously, some have referred to these procedures as "minimally invasive" or "percutaneous" therapies, these terms should only be used where appropriate. Minimally invasive therapies refer to all therapeutic procedures that are less invasive than open, conventional surgery. All percutaneous procedures are therefore minimally invasive, however, not all minimally invasive therapies are performed or applied percutaneously. Indeed, the term "minimally invasive" is often used by surgeons to refer to procedures performed via mini-laparotomy or with laparoscopy [7]. Although less invasive than open surgery, these are clearly more invasive than percutaneous image-guided tumor ablation procedures. Including the term "percutaneous" as a prefix to image-guided tumor ablations is often too limiting as it does not reflect the fact that tumor ablation procedures can also be performed laparoscopically, endoscopically, or at surgery [8, 9].

Individual procedures and therapies have often received multiple different names by various investigators, which can potentially lead to confusion. Hence, we propose and recommend a unified approach to the terminology regarding these therapies. The primary aim of this classification is to provide simplicity and clarity, most notably by eliminating extraneous detail and many acronyms. In general acronyms are to be avoided whenever possible.

The methods of tumor ablation most commonly used in current practice should be divided in to two main categories: a) **Chemical Ablation** and b) **Thermal Ablation**. These require further definition and standardization of terminology as outlined below. Other interventional oncologic therapeutic approaches including the percutaneous delivery of genetic material and radioactive seeds, and the transcatheter delivery of chemoembolization [10, 11] may ultimately require better definition, but are beyond the scope of this current position paper. Nevertheless, many of the issues discussed concerning reporting criteria, will likely be equally appropriate for clinical trials with those therapies.

Chemical Ablation [12 – 14]:

These therapies should be classified based-upon the universally accepted chemical nomenclature of the agent(s) such as ethanol, acetic acid, etc. that induce coagulation necrosis and cause tumor ablation. For example, the term ethanol ablation should replace PEI (percutaneous ethanol instillation or injection), PAI (percutaneous alcohol instillation), and others [12, 13]. When reporting results, the route (IV, intra-arterial, or interstitial), substances injected, delivery vehicle (size and type of needle or catheter), and rate of delivery (rapid injection or a defined rate of infusion) should be specified in the materials and methods section of the manuscript. The term "instillation" for the direct delivery of pharmacologic agents is preferred given that many pharmaceuticals can be injected (a process that implies rapid percutaneous delivery) or delivered intravascularly via a catheter.

Thermal Ablation Procedures [15 – 45]:

This category includes energy sources that destroy a tumor with thermal energy, either by heat (RF, laser, etc.) or by cold (cryoablation). For thermal therapies energy is "applied". The term "Irradiation of energy", particularly in regard to microwave ablation is a misnomer, and should therefore be avoided.

Procedure Terms:

We prefer to use the term "**procedures**" rather than "operations". The latter implies open surgery. A treatment may consist of one or more procedures. The term "**session**" is often used to describe cases in which several procedures (or sessions) are needed for the tumor to be adequately treated. Each manuscript should state clearly how many procedure sessions were needed and why.

Energy applicator: Although the devices are often referred to as "needles" or other non-specific terms, they do not always conform to these precise classifications. Hence, the term "**applicator**" should be used when generally describing all devices. For precision, RF applicators are "**electrodes**", microwave applicators are "**antennas**", and laser applicators are "**fibers**". By convention and consensus "**cryoprobes**" are used to freeze tissue during cryoablation.

Energy sources:

1. **Radiofrequency Ablation**: This term applies to coagulation induction from all electromagnetic energy sources less than 900 KHz, although most currently available devices function in the 375 – 500 KHz range [15]. The term Radiofrequency should be written as a single non-hyphenated word and can be abbreviated as "RF". Most devices currently used are monopolar in that there is a single "active" electrode, with current dissipated at a return grounding pad. Bipolar devices have two "active" electrode applicators, usually placed in close proximity to achieve contiguous coagulation between the two electrodes [16]. Additionally, many electrode modifications are now available, as classified below. The type of device and electrode used clearly influences the extent of ablation. Hence, clarity and standardization of terminology is required.

   i. **Multi-tined, expandable electrodes**: This standard terminology refers to a family of electrodes that are currently available from several manufacturers [8, 9, 17 - 20]. The usual embodiment of this type of device is that of an array of multiple electrode tines that expand from a single centrally positioned larger needle cannula. Currently these are being referred to as umbrella electrodes, multi-tined electrodes, Christmas tree electrodes, multiple hooked electrodes, or arrays, but this has led to confusion. Given the number of electrode types that have recently become available, the exact electrode model must be specified.

   ii. **Internally cooled electrodes**: Some devices have a perfusate (such as saline or water) that flows in internal lumena which does not come in direct contact with patient tissues [21 - 23]. These should be referred to as "internally cooled electrodes" (single or cluster [not "clustered"]), and not confused with perfusion electrodes, as described below. The term "cluster electrode" is most appropriate to describe internally cooled electrode devices in which three or more closely spaced (<1 cm) electrodes are used simultaneously to approximate a larger diameter electrode [24]. Many refer to these electrodes as "an array", which may not adequately reflect the true underlying mechanism for enhanced energy deposition and ablation.

iii. **Perfusion electrodes**: Electrodes that have small aperatures at the active tip allowing fluids (i.e., normal or hypertonic saline) to be infused or injected into the tissue before, during, or after the ablation procedure should be referred to as perfusion electrodes [25, 26]. The term replaces descriptions such as "cool-wet" or "wet" electrodes.

iv. **Algorithm of energy deposition**: The methods used for applying energy have undergone continuous modification and improvement, which has led to substantial confusion and difficulty comparing the results of studies performed by different groups of investigators. When reporting results, pulsing techniques and other methods for amplifying energy deposition should be succinctly elaborated upon in the materials and methods. Whenever possible a reference for the precise algorithm used (e.g., ramped energy deposition [18], or impedance regulated [27]) and the model number of the generator should be cited. Additionally, other parameters including the use of monopolar or bipolar systems, the amount of energy applied (current and/or watts), and the duration of ablation should be provided.

v. **Adjuvant therapies**: Increased use of adjuvant therapies such as the concomitant percutaneous instillation of sodium chloride solutions to alter electrical and thermal conductivity during ablation are being reported with many variations in technique [28, 29]. Hence, specific details of the adjuvant used (i.e., drug concentration, route and rate of administration, timing in relation to ablation therapy, etc.) must be provided. Whenever possible a reference for the precise algorithm and the rationale for the selected adjuvant therapy used should be provided.

2. **Laser Ablation [30 - 34]**: The term "**laser ablation**", should replace terminology such as "laser intersitital tumor therapy", "laser coagulation therapy", and "laser interstitial photocoagulation". This term should be used for all types of ablation using light energy. Given multiple laser technologies and application methods, including superficial therapy (contact/non-contact mode) or transcutaneous ablation, the term "interstitial" can be reported to clarify that laser energy is applied via fibers directly inserted into the tissue.

In addition to the laser source (Nd:YAG, Erbium, Holmium etc.) and precise wavelength, additional device characteristics must be specified, including: a) type of laser fiber (flexible / glass dome); b) modifications to the tip (i.e., flexible diffusor tip, or scattering dome) with dimensions and materials specified; c) length of applicator and diameter of the optic fiber; and d) the number of laser applicators used (i.e., single versus multiple applicators). Similar to the reporting requirements for RF ablation, additional details of device modification such as pulsing algorithms and internal cooling of the applicator should be provided as well. The following technical parameters also should be provided: a) laser power, reported as Watts per cm active length of laser applicator; b) total duration of energy application; c) total amount of energy applied per tumor (mean and range); and d) sequential or simultaneous energy application to multiple fibers. For energy applied, in addition to the energy measured before the laser enters the fiber, ideally the actual energy output of the fiber/dome prior to the ablation and/or at the end of the procedure should be measured.

3. **Microwave Ablation**: This term should be used for all electromagnetic methods for inducing tumor destruction using devices with frequencies greater than or equal to 900 KHz [35 - 37]. The term "microwave ablation" should replace the less succinct terminology of "percutaneous microwave coagulation therapy" or "microwave coagulation therapy". Additionally, the precise frequency of the device and the type of applicator(s) should be provided.

4. **Ultrasound Ablation**: There are currently two methodologies for the application of ultrasound energy – extracorporeal (or transcutaneous) [38] and direct (or percutaneous) via a needle-like applicator [39]. Hence, additional nomenclature is required. The term "**High Intensity Focused Ultrasound**" (HIFU) or "Focused Ultrasound" should be reserved for describing the extracorporeal method, whereas "percutaneous ultrasound ablation" denotes the placement of an applicator within the target. (Here the term "percutaneous" is necessary.)

5. **Cryoablation**: This term should be used for all methods of destroying tissue by the application of low temperature freezing [40 - 45]. The term "cryotherapy" is a suitable alternative as it has been used for many years to describe these methods, and it may also be useful when conducting a literature search on this subject [44]. The phrase "cryo" as a freestanding term is to be avoided, as "cryo" is a prefix and not a word. The archaic term "cryosurgery" is also to be avoided as imprecise given the introduction of newer applicators that can be introduced percutaneously in a minimally invasive fashion.

   Freezing of tissue with rapid thawing leads to the disruption of cellular membranes and induces cell death [45]. In the past, liquid nitrogen was placed directly on tissue, but with the exception of dermatologic applications, this method is no longer used. In the neck, chest, abdomen/pelvis, and extremities, cryoablation is performed using a closed cryoprobe that is placed on or inside of a tumor. The two main types of systems use either gas or liquid nitrogen, or argon gas. Temperatures are measured either at the tip of the cryoprobe, or in the handle. In the past, temperature readings from cryoprobes have been a source of controversy as some manufacturers measure the temperature of the coolant as it enters the distal probe tip, and others measure at the probe tip itself. Hence, the temperatures at which cryoablation is performed should be specified. For publication purposes, the type of cryoablation system, the gases used, probe dimensions, length and number of freeze- thaw cycles (active or passive thawing) should also be specified.

Terminology for describing the effects of blood flow: All of the thermal methods are negatively influenced by blood flow as it can potentially remove heat before complete tumor ablation is achieved [1 - 6]. (This is also true in reverse for cryoablation where the premature warming of tissue by blood can limit the effects of freezing on tissue). The term "**heat sink effect**" refers to cooling by adjacent visible (>1 mm diameter) blood vessels when ablated tissues are heated [46 - 48]. In effect, the shape of the thermal lesion is altered away from the vessel and the overall lesion size is diminished due to removal of heat or cold by flowing blood [46 - 47]. Although these phenomenona serve to protect blood vessels and prevent bleeding from large vessels, they are also a major source of incomplete tumor ablation in many studies involving both thermal and cryoablation. "**Perfusion mediated tissue cooling (or heating)**" is a more encompassing term that refers to both the effects of the larger heat sinking vessels as well as the substantial effects of capillary level microperfusion [48]. Several strategies have been developed to overcome this problem, ranging from pharmacologically decreasing blood flow [49], to temporary vascular balloon occlusion of a specific vessel during ablation (i.e., hepatic artery, hepatic vein, and/or portal vein during intrahepatic ablation) [50], to intraarterial embolization and chemoembolization [36, 51, 52], to performing a Pringle maneuver at laparotomy [9, 47].

B. Image-guidance

While all procedures referred to in this communication refer to tumor ablations guided by imaging, it is important to understand what is meant by the term "image-guidance". First, *guidance* refers to procedures in which imaging techniques (e.g., fluoroscopy ultrasound, CT, and MRI) are used during the procedure. Imaging is used in five separate and distinct ways: planning, targeting, monitoring, controlling, and assessing treatment response [53]. Treatments are planned before the procedure, and the assessment of treatment response occurs after the procedure is completed. Targeting, monitoring, and controlling are all performed during the procedure. The meaning of these terms are described further as follows:

1. **Planning**: Imaging techniques, including ultrasound, CT, MRI, and more recently PET, are used to help determine whether patients are suitable candidates for these procedures. Imaging aspects that are particularly important include tumor size and shape, number, and location within the organ relative to blood vessels, as well as critical structures that might be at risk for injury during an ablative procedure. Modalities such as PET/CT, and three- dimensional reconstructions of cross-sectional imaging data may be used more often in the planning of image-guided tumor ablations in the future.

2. **Targeting**: This term is used to describe the step during an ablation procedure that involves placement of an applicator (e.g., an RF electrode or cryoprobe) into the tumor. While much of the current image-guided tumor ablation literature describes the use of techniques such as ultrasound and CT to target tumors for purposes of ablating them, targeting is only one aspect of intraprocedural image-guidance. Ideal qualities of a targeting technique include those with real-time imaging, multiplanar capabilities, and those that can be used interactively. For example, ultrasound [54] and some MRI systems [55, 56] have all of these qualities.

3. **Monitoring**: Monitoring is the term that is used to describe the process by which therapy effects are viewed during a procedure. Changes in imaging that occur during a procedure can and should be used to determine treatment effects. Important aspects of monitoring include how well the tumor is being covered by the thermal therapy, and whether any adjacent normal structures are being affected at the same time. Not all image-guidance

techniques provide the same degree and types of monitoring. For example, MRI is currently the only modality with well-validated techniques for real-time temperature monitoring [40, 57 – 59]. The term “monitoring” should not be used to describe response to treatment; for this, “treatment assessment” or “follow-up” is used.

4. **Controlling**: This term is used to describe the intraprocedural tools and techniques that are used to control the treatment. In order to control an image-guided ablation procedure, the treatment should be monitorable, such that the operator can utilize the image-based information obtained during monitoring to control it. This may simply be repositioning of a therapy applicator based upon physican experience, imaging findings, and thermal feedback, or it could be as sophisticated as an automated system that automatically terminates the ablation at a critical point in the procedure [60].

5. **Assessment of Treatment Response**: Imaging used to assess an image-guided tumor ablation procedure occurs after the procedure is completed and is discussed below as post procedural imaging [1 – 6].

C. Pathology and Imaging:

1. The difference between pathologic findings and imaging findings must be stressed by the appropriate selection of terminology. Although in many cases there is a good correlation or overlap between radiologic and pathologic findings, this is not invariably the case as over- and under-reporting of the true extent of disease has occurred [61, 62]. The classic example of this is assuming that imaging findings (i.e. the zone of abnormality on the image) are equivalent to the pathologic findings (i.e. the true zone of tumor destruction / treatment effect), which may not always be the case. Hence, careful differentiation between imaging findings and findings at pathology must be made. This distinction is critical given that our accuracy at assessing the extent of tumor destruction by imaging is limited by the resolution of imaging.

   a. **Zone of cell death at pathology**: This should be referred to as “**coagulation**” or “**coagulation necrosis**”. Given that many tumors undergo central necrosis without ablation therapy, the term “coagulation” is preferred over the use of “necrosis” alone, as it denotes that the ablation intervention is actively leading to tumor destruction. The term “coagulative necrosis” should certainly be avoided given the fact that it is now well accepted that the zone of coagulation, while predominantly comprised of coagulative necrosis, does not have the classic, well defined histologic appearance in the acute period or even within some zones of adequately ablated tissue many months following ablation [22, 61, 63]. Indeed, in many cases specialized stains are required to confirm that cellular death has been achieved after thermal ablation [61].

   Another important issue is defining the zone of ablation at gross pathology. Most thermal therapies induce a central “white zone” of coagulation, a pathologic finding that is generally accepted to represent coagulated tissue, surrounded by a variable “red zone” of hyperemia which is most often absent in *ex vivo* specimens [64]. However, there has been controversy in measuring and hence comparing the "true" size of induced zones of ablation based upon the fact that some have reported that this more peripheral "red" zone also represents ablated tissue and include it in their measurements. To avoid confusion, both measurements (white alone and "white plus red") should be provided. At a minimum, the zones included in gross pathologic measurement should be specified.

b. **Zone of ablation at post-procedural imaging**: Appropriate terminology must reflect the fact that although we rely on imaging to define the gross extent of induced coagulation, our accuracy is limited by both spatial and contrast resolution to approximately 2 – 3 mm (depending on the imaging modality employed) [61]. Hence, in truth post-procedural imaging findings are only a rough guide to the success of ablation therapy as microscopic foci of residual disease by definition cannot be expected to be identified. The term "ablation zone" can be used to describe the radiologic region or zone of induced treatment effect (i.e., the area of gross tumor destruction visualized by imaging). The term "lesion" is to be avoided given potential confusion as to the intended meaning as the term "lesion" has been used to refer to both the "ablation zone" as well as the underlying tumor to be ablated itself.

   There are two types of imaging findings that are identified following an ablation procedure, those related to zones of decreased perfusion, and those in which the signal intensity (at MRI), echogenicity (at ultrasound), or attenuation (at CT) are altered [1 - 6]. Hence the imaging strategy employed and the criteria used to define ablation must be specified. For contrast enhanced studies, it is important to recognize that in some organ sites, particularly the kidney, minimal contrast enhancement (i.e., for CT $<$ 20 Hounsfield units) early post-ablation, can be identified in areas that are subsequently proven at pathology to be uniformly dead tissue [65]. (This finding is not well understood but may be due to pseudoenhancement, as has recently been described for renal cysts, or alternatively to represent true minimal enhancement from leaky capillaries at the treatment margin.)

Other imaging findings require precise definitions as well:

i. **Transient hyperechoic zone**: is the preferred term to describe the transient (up to 30 – 90 minutes) zone of increased echogenicity seen by ultrasound within and surrounding a tumor during and immediately after RF ablation [66, 67]. Thereafter, tumors that are treated often become of mixed echogenicity on follow-up scans. This finding is felt to represent microbubbles forming from tissue vaporization during active heating, and is most often used as a rough guide as to the extent of induced tumor destruction. However, it is not a precise marker as both under- and overestimation of the true extent of coagulation have been reported. This term should replace imprecise terminology such as "Ultrasound cloud", "Ultrasound storm", "outgassing", and "microbubble vaporization".

ii. **Ablative margin**: For many disease processes, particularly for tumors in the liver, the ablation of appropriate margins beyond the borders of the tumor is necessary to achieve complete tumor destruction. The term "ablative margin" is proposed to describe the 0.5 – 1.0 cm region that should ideally be ablated in these cases [68]. This term is preferable to “surgical margin” (as there is no surgery). It is important to stress that this extent of treatment is not always necessary or desired, particularly when attempting to destroy focal lesions in the kidney in patients having a tendency toward the development of multiple tumors (such as those with Von-Hippel-Landau) where nephron sparing and more limited ablation is desired to preserve renal function and avoid dialysis [65].

For normally vascular organs such as the kidney and liver, creation of an ablative margin results in zones of low attenuation and absent perfusion extending into the parenchyma [1 - 6]. Increased attenuation occurs in low density tissues such as perinephric fat (for exophytic renal tumors) [65, 69], and in the lungs where the term “ground glass opacity” is used to describe the imaging findings of the treatment zone surrounding and including the ablated lung tumor [70].

iii. **Benign peritumoral enhancement**: This finding can be seen at both pathology and on contrast enhanced imaging and typically represents a benign physiologic response to thermal injury (initially reactive hyperemia and subsequently fibrosis and giant cell reaction) [61]. Depending on the protocol used for contrast enhanced imaging (injection rate and scanning delay), this transient finding can be seen immediately following ablation and can last for up to 6 months in duration post-ablation. This finding usually manifests as a thin rim, or penumbra, can typically measure up to 5 mm acutely, but most often measures 1 – 2 mm. It is a relatively concentric, symmetric, and uniform process with smooth inner margins that needs to be differentiated from “irregular peripheral enhancement”. The finding is most readily appreciated on the arterial phase for CT, with persistent enhancement often seen on delayed images at MRI.

iv. **Irregular peripheral enhancement**: represents residual tumor occurring at the treatment margin. In contrast to “benign peritumoral enhancement”, residual unablated tumor often grows in scattered, nodular, or eccentric pattern. This sign indicates incomplete local treatment (i.e., residual unablated tumor). As such, if not subject to further therapy these foci tend to continue to grow. Given the delayed enhancement characteristics of many hypovascular tumors, often this finding is best appreciated by comparing portal venous or delayed (3 or more minutes following contrast injection) images to baseline images.

v. **Involution of coagulation**: The term “involution” should describe the process by which the body eliminates the zone of induced coagulation over time. The term “shrinkage” should be avoided as being imprecise. The term “regression” is likewise to be avoided given that it is commonly used in the medical oncology literature to describe involution of just the tumor itself, rather than the induced coagulation that often involves both tumor and the surrounding tissues (i.e., the ablative margin).

vi. **Other imaging findings**: Many other imaging findings representing both host reaction to ablation and repair mechanisms will undoubtedly be seen and reported including: inflammatory stranding in the acute period following ablation, and more chronic findings such as fibrosis, scarring, and architectural distortion. In general, despite the tendency towards creative description, previously standardized radiologic nomenclature should be used to describe these findings whenever possible. The number of new terms to describe these processes should be minimized to where new descriptive terminology imparts prognostic value (such as differentiating between benign peritumoral enhancement and residual unablated tumor).

2. **Reporting of tumor and ablation size**: Appropriate uniform guidelines and standards are needed for the reporting of the extent of induced coagulation. In the past, comparison between technologies has been made somewhat difficult based upon the fact that some authors report the largest diameter of induced coagulation, others report the average diameter, while some report the short axis diameter. Additionally, coagulation has occasionally been reported as a volume of ablated tissue without any definition of dimensional measurements. Hence, uniform standards of comparison are essential and must be adopted.

   "Index tumor" is the preferred term for the initially identified tumor prior to ablation. This tumor should not be referred to as a "lesion" as this term could be confused with the zone of induced coagulation or the region of ablation at imaging.

   Size classification of tumors: Actual tumor sizes (mean ± standard deviation, and range if applicable) should be reported. Given that appropriate ablation of adequate margins often represents the rate-limiting step for treatment efficacy, the maximum diameter of the original tumor must be specified. However, many investigators perform analyses of their results based upon stratification of tumor sizes. In this regard, currently, there is too much ambiguity and variability in the categorization of tumors by size. Different investigators have reported an upper limit of 2, 2.5, 3, and 5 cm as "small tumors", and 5 or 10 cm as large. This has made the direct comparison of results using different technologies challenging. We therefore recommend that if such categorization is performed that the tumor size classification should be standardized according to the following scale: small tumors as = 3 cm in diameter; 3 - 5 cm tumors as intermediate; and tumors > 5 cm as large. This classification was determined as most practical since it parallels the current technical capabilities and efficacy for most image-guided ablation therapies.

   Comparing zones of coagulation among different ablation techniques: Often the extent of induced coagulation is reported in experimental studies as a vehicle for comparing different ablation technologies and parameter modifications [71, 72]. The extent of induced coagulation should include reporting of the short axis diameter, given that this parameter influences the overall extent of necrosis that can be achieved from a single application of energy, and is likely to be an important factor influencing technical success in clinical practice. Hence, while additional parameters can certainly be provided and may be potentially useful, at a minimum this should be the standard that is reported to enable honest comparison between techniques. Of course given that the ablation of a tumor is performed in three dimensions (i.e., it is a volumetric problem), ideally, all three-dimensional measurements of the ablation zone and tumor, and less ideally both measurements of the cross-sectional area should be provided. If volume is to be used as the only reported parameter, then a rationale must be specified. Average diameters should only be accepted if the tumor or zone of ablation is truly spherical, varying not more than 2 – 3 mm in cross-sectional diameter. It is further well known that many devices produce irregularly shaped zones of coagulation. Hence, the degree of uniformity or irregularity in the shape of the ablation zone should be specified.

It is important to stress that reliance on minimum and maximum sizes for the zone of ablation may not be useful for predicting clinical technical efficacy as other technical factors are likely to be equally important. For instance, depending on the orientation of the energy applicator, a 1 x 2 cm tumor may be adequately treated by a 2 x 3 cm zone of ablation, but not by a 3 x 2 cm zone of ablation. Ablation diameter or volume may also not tell the entire story. Although a 3cm zone of coagulation may completely cover a 2cm tumor when correctly positioned, if off the mark, it will fail to destroy the entire tumor.

D. Standardization of follow up:

Currently, defining appropriate length of follow up and the time points for defining technical success are not well established. One investigator's long-term follow up is often another's short-term follow up. Hence, specific guidelines need to be adhered to dependent on the type of disease treated, and the intended goal of the study. Treatment study goals are generally related to one or more of the following four categories: (1) "**technical success**", or was the tumor treated according to protocol ?, (2) "**technique efficacy**", or was the tumor effectively ablated? (3) morbidity, or were critical structures and complications avoided? , and (4) outcomes, or was there some improvement in survival, quality of life or palliation ?

1. **Technical success**: This term simply adresses whether the tumor was treated according to protocol and covered completely. Tumor coverage can be assessed either during or immediately following the procedure. For example, MRI can be used to monitor thermal injury and can be used to show that the tumor is being covered completely during the procedure. In CT, a contrast-enhanced CT can be performed immediately after the ablation. A tumor that is treated according to protocol and covered completely as determined at the time of the procedure is "technically successful". The importance of this term is to help investigators separate out those patients in whom the protocol could not be executed completely, either for technical reasons or for reasons related to comorbid disease, from those that were treated according to protocol.

2. **Technique efficacy**: Distinction between "technical success" and "technique efficacy" must be made. Efficacy can only be demonstrated with appropriate clinical follow up. "Technique efficacy" should therefore refer to a prospectively defined time point (i.e., immediately following the last course of a defined ablation protocol, 1 week, or 1 month after treatment) at which point "complete ablation" of macroscopic tumor as evidenced by imaging follow-up (or another specified endpoint) was achieved. The number of sessions (i.e., the number of interventional procedures) to achieve the specified endpoint should likewise be defined. Authors are encouraged to report whether or not this complete ablation included an ablative margin.

   Comparison of technical success and efficacy between various ablation protocols has been challenging as many authors have adopted different terminology or guidelines. This problem is further compounded by our ability and often the clinical need to ablate a tumor over many sessions and the possibility of ablating growing foci of local tumor progression months after the initial course of therapy. We therefore recommend defining a window of initial therapy for each ablation technique during which it is reasonably expected for the tumor to be completely ablated. For percutaneous thermal ablation, ideally this should not exceed an upper limit of either 1 – 4 sessions, or a specified time frame (up to one to three months), depending upon the size, type, and location of the tumor, as well as the rationale for therapy. *We have purposefully left definition of this endpoint as a broad range, given the committee's inability to achieve consensus on defining more specific parameters for each disease process at this time.* If complete ablation cannot be achieved within these specified parameters, the tumor should be classified as "unsuccessfully treated".

Primary and Secondary technique efficacy rates: Given that multiple sessions of image-guided tumor ablation therapy are often given over the course of the disease), primary and secondary technique efficacy rates should be reported. The "**primary efficacy rate**" is defined as the percentage of tumors successfully eradicated following the initial procedure or a defined course of therapy. The "**secondary or assisted efficacy rate**" is defined as including tumors that have undergone successful repeat ablation following identification of local tumor progression. The term "**retreatment**" should be reserved for describing ablation of locally progressive tumor, in cases where complete ablation was initially thought to have been achieved based upon imaging demonstrating "adequate" ablation of the tumor.

The technical success and technique efficacy rates are very important as we define the limitations of our technologies, ideally in a manner similar to other disciplines (i.e., surgical resection papers typically report a positive margin rate). Nevertheless, for some protocols the concepts of local technical success, and local tumor progression (i.e. technique efficacy) may have limited impact on the most important outcome parameter – patient survival. For example, using 3-4 sessions or one month as the window may be of secondary importance if the patient lives for five years because of the treatment, or if the tumor is completely eradicated over multiple courses of ablation therapy over many years.

Complete ablation versus partial ablation. Many reports have surfaced in which different degrees of partial ablation have been reported [22, 30, 33, 73, 74]. While consensus has been achieved for defining complete and incomplete ablation, there has been a rather arbitrary definition of incomplete ablation. For example, some have reported nearly complete ablation as representing greater than 90% induced necrosis, while others have used a threshold of 95% necrosis of the index tumor. Nevertheless, it is the opinion of the majority of the committee that this kind of classification of partial ablation is not warranted, in an overwhelming majority of cases given that adequate data is lacking to support a difference in outcome between different levels of partial ablation. Furthermore, such percentages are often estimates and may be inaccurate. Hence, at this point in time, such stratification should be avoided. It is important to stress that the elimination of this type of stratification does not negate the utility or imply the lack of benefit of tumor ablation as a palliative method. However, other end points should be chosen (see below) when reporting these cases based upon the rational of palliation.

Tumor Palliation: The specified well-defined rationale for palliative therapy must be provided and an appropriate methodology for assessing outcomes must be provided. For example, if tumor ablation is valid as a vehicle for pain reduction, pre- and post-procedure pain scales should be obtained [75, 76]. If ablation is employed to reduce symptoms of a syndrome (such as carcinoid or other hormonally active or paraneoplastic tumors [77]), appropriate documentation of laboratory results from blood or urine pre- and post-therapy must be provided, and other symptomatic endpoints and grading systems must be specified and employed. Needless to say, one cannot "palliate" asymptomatic tumors. Hence, the term "**debulking**" should be used when describing a procedure performed with the sole intent of inducing a reduction of tumor burden.

Failure of Therapy:

i. **Causes of treatment failure**: The distinction between local incomplete therapy (tumor progression), new foci of disease within the target organ (especially the liver), and distant malignancy should be distinguished whenever possible and reported upon. Discrimination between "local tumor progression" and new tumor is important for determining the potential utility (i.e., local treatment success rate) of a given method, in the setting of many potentially confounding causes for the demise of a given patient. Additionally, for patients with cirrhosis, the causes of mortality should be differentiated between hepatic disease and others.

ii. **Local tumor progression**: Many have used the term "local recurrence" to describe the appearance over follow up of foci of untreated disease in tumors that were previously considered to be completely ablated as local recurrence. This is often a misnomer given the fact that the tumor in essence did not recur, but was never completely treated. Hence, the process often described is in actuality "residual unablated tumor". However, in many cases it is virtually impossible to determine whether there was incompletely treated viable tumor that continued to grow, or if a new tumor (or in the case of HCC, "daughter" or "satellite" lesions) grew at the original site. Given this reality, "local tumor progression" is the preferred terminology over "local recurrence".

Patient mortality: Given the oncologic population most often treated, substantial patient mortality that is unrelated to the ablation intervention is anticipated, particularly in clinical studies with long-term follow-up. As such, the cause of death should be specified as "tumor-related" or due to "other-causes". For "tumor-related" death, further sub-classification, if possible (for example differentiating death due to hepatic or diffuse metastatic burden) will often be useful, as it can potentially shed further light on the efficacy of therapy. Any patient death within 30 days of image-guided tumor ablation should be addressed.

3. Complications [78 – 79]:

A unified standardized grading system should be adopted as proposed here, as modified from prior accepted complication scales [80, 81]. The definition of death is self-explanatory and should be reported on a per patient basis. The specific cause of death should be reported, with the potential and degree of causality to the ablation procedure clearly specified. Major and minor complications, and side effects should be reported based upon the number of ablation sessions on a per session basis. However, ideally, the number of ablations performed should be included, as multiple ablations increase the likelihood of complications [78, 79].

The definition of major complications are those that if left untreated might threaten the patient's life, lead to substantial morbidity and disability, or results in hospital admission or substantially lengthens the hospital stay. This includes any case in which a blood transfusion or interventional drainage procedure is required. All other complications are considered minor. It is important to stress that several complications such as pneumothorax or tumor seeding can be either a major or minor complication depending on severity. For tumor seeding this would depend upon whether or not the ectopic tumor focus can be successfully ablated or otherwise treated.

Differentiation between immediate complications (up to 6-24 hrs following the procedure), peri-procedural complications (within 30 days), and delayed complications is advised. This stratification will give the reader an idea when specific complications/side effects are most likely to occur and assist in defining when and how to take adequate precautions. Ablation related complications should include problems encountered within the peri-procedural (30 days) time period that can be related in any way to the procedure, as well as additional complications that were identified at delayed follow-up imaging that were judged to be highly likely due to the ablation therapy (biliary ductal stricture, tumor seeding along the needle tract, etc.). Additionally, it should be specified which complications are being reported on a patient-by-patient basis (such as death) and for which the denominator represents the number of sessions, or by the number of tumors.

Side effects are common undesired consequences of the procedure that although occurring frequently, rarely if ever result in substantial morbidity. These include pain, the post-ablation syndrome, and asymptomatic pleural effusions and minimal asymptomatic perihepatic (or renal) fluid or blood collections seen at imaging. Another such side effect would include asymptomatic imaging evidence of minimal thermal damage to adjacent structures without other evidence for negative sequelea ("i.e., collateral damage"). An example of this would include when the zone of ablation extends beyond the liver capsule to include small portions of the diaphragm or kidney.

Pain: Even with appropriate conscious sedation techniques, patients may experience pain during ablation procedures. Additionally, a substantial minority of patients experience pain for several days, occasionally lasting one to two weeks following an ablation procedure. Lastly, thermal ablation, particularly RF, is being used with increased frequency as a method for treating refractory metastatic and primary bone tumor pain [75, 76]. We therefore propose adopting the NCI Common Toxicity Criteria for the reporting of pain (This NCI document can be downloaded from the website http://ctep.cancer.gov/reporting/ctc.html) [82]:

Grade 0: no pain
Grade 1: mild pain not interfering with function
Grade 2: moderate pain: pain or analgesics interfering with function but not interfering with activities of daily living.
Grade 3: severe pain: pain or analgesics severely interfering with activities of daily living.
Grade 4: disabling pain.

Post-ablation syndrome: This syndrome is a transient, self-limiting symptom/sign complex of low-grade fever and general malaise [44, 83]. The duration depends on the volume of necrosis produced and the overall condition of the patient. If small areas are treated the patient is unlikely to experience post ablation syndrome at all. If very large areas of liver tumors are ablated, the syndrome may persist for 2 -3 weeks. The majority of patients who get this syndrome will experience some malaise for 2 - 7 days depending upon the volume of tumor and surrounding tissue ablated and the integrity of the patient's immune system (i.e., patients on steroids or with small tumors may have no post ablation syndrome).

4. **Follow-up and Outcomes**:

a. **Imaging follow-up**: Currently, despite a reliance on imaging findings to determine the extent of "unablated residual tumor", there is a lack of consensus on a standard follow-up interval regimen for imaging. The most common approach taken by members of the working group include contrast-enhanced CT or MR imaging within 6 weeks of the initial ablation to determine whether or not additional ablation therapy is required (many centers perform this on the day of the initial procedure), and thereafter every 3 - 4 months, to determine technique efficacy. Imaging intervals may also vary depending on the type of underlying tumor and the goals of treatment. At a minimum, the intervals at which imaging follow-up were obtained should be clearly specified.

Although standard imaging criteria for response assessments have been defined for evaluation of other cancer therapies, these criteria focus almost exclusively on tumor size [84]. However, given the heavy reliance on morphologic features other than size when assessing results of ablation therapy, exclusive reliance on tumor size does not provide a complete imaging assessment of tumor response. Therefore, in addition to reporting index tumor diameter and the diameter of the zone of ablation, assessment of tumor enhancement or lack thereof should also be included in the imaging response assessment following ablation therapy.

b. **Length of Follow-up**: Currently, the majority of published studies for most tumor ablation technologies are preliminary and have only a limited number patients with longer periods of follow-up. However, ideally, we will need studies in which large numbers of patients are followed. When assessing survival and disease-free survival, an appropriate length of follow up should be selected based upon tumor biology and accepted criteria for other therapies for a given tumor type. For example, the surgical literature has required long term follow up of greater than 5 years for determining the impact of various therapies on survival for colorectal metastases to the liver or hepatomas [85 - 87]. For other tumors, the appropriate length of follow up may vary, and indeed for more rapidly growing tumors such as in the lung, the length of follow up may be shorter. For slow growing tumors, such as primary renal cell carcinoma, the length of follow up may need to be longer. As a general rule, we advocate for the rapid establishment of a consensus on acceptable follow-up times for different tumors. Regardless, based upon these concerns, we recommend reporting the actual mean and/or median length of follow up (with ranges and/or standard deviations, as appropriate) rather than arbitrary classification into short, intermediate, or long.

D. Other important aspects requiring attention when reporting clinical results:

1. Technique parameters to be provided for publication:

It is our belief that many published series do not provide enough technical detail to permit duplication of the investigators' efforts. This problem is compounded by the fact that there are many different types of ablation equipment on the market and in development, and these often change. Hence, the specification of the parameters such as duration of application energy applied, manufacturer, etc. must be provided. Also, the number of treatment sessions for each tumor should be specified. The procedure approach (i.e., whether the procedrue was performed percutaneously, laparoscopically, or endoscopically) should also be clearly specified. Additional parameters to be provided for publication should include: a) whether the procedure is performed under general anesthesia or conscious sedation (the specifics of anesthesia and medications administered during the procedure and in the recovery phase should be always be reported, including agent, dose, route, etc.); b) the types of imaging guidance (CT, CT fluoroscopy, ultrasound and or MRI); c) whether or not the patient was hospitalized; d) the number of sessions required to initially achieve technical success; and e) the subsequent rates of other tumors requiring additional ablation therapy. Lastly, any repositioning of the applicator during the ablation and the procedure for applicator removal (i.e., use of fiber enclosure, or other closure devices) should be noted.

2. **Other study population data to be reported**: The study population should be rigorously described, including inclusion/exclusion criteria, and tumor type and size. The degree of proof of disease required for entry into the study (i.e., biopsy, imaging, or serologic criteria) should be clearly specified.

   Recent studies have also suggested the potential complementary effects of chemotherapy and radiation therapy on ablation efficacy [88]. Hence, the administration of either of these therapies to patients enrolled in clinical trials of ablation should be specified. This should be further classified as having received the conventional oncologic therapies previously, around the time of ablation (within one month), or during the follow-up period. The specific therapy protocol and the duration of therapy in relation to the ablation therapy should also be provided.

3. **Accurate and complete delineation of ablation procedures**: Substantial confusion and difficulty in comparing results has arisen regarding the success and complication rates due to the fact that patients may have had one or more tumors treated over multiple procedure sessions. Ideally, all four parameters (number of patients, tumors, treatment sessions, and ablations) should be reported whenever possible. Additionally, results are often reported for heterogeneous populations of patients for which varied rationales for the procedure (i.e., cure vs. palliation) or outcomes (i.e., hepatic metastases vs. hepatocellular carcinoma) have been reported. Stratification of patients into appropriate categories is therefore advised to avoid confusion and best facilitate extraction of clinically meaningful conclusions.

4. **Minimizing Technical Jargon**: Although substantial technical jargon and marketing terminology appears within our literature, these should not be used. For example, colloquial phrasing such as "lesioning" and "burning" are to be avoided when describing the application of thermal energy. Another example is the concept of "roll off" to describe the impedance control algorithm of a device of one particular manufacturer. The term "roll off" that

describes the impedance control algorithm of a particular manufacturer's RF device should not be used.

Conclusions:

The intent of this position paper is to provide an appropriate vehicle for standardizing the reporting of the various aspects of image-guided ablation therapy. Based upon a mandate from the International Working Group on Image-Guided Ablation Therapy, our intent and mission is to provide such a framework in order to facilitate the clearest communication between investigators, and the greatest flexibility in comparison between the many new, exciting, and emerging technologies. Clearly, this is an ongoing process that will require modification as our understanding of these technologies improves, new treatment paradigms emerge, and greater consensus is achieved on standardizing the reporting of outstanding issues. Nevertheless, we strongly encourage all of our colleagues to adopt the terminology and reporting strategies outlined in this position paper, as our working paper represents a document overwhelmingly adopted by the International Working Group on Image-Guided Ablation Therapy at RSNA 2002.

Appendices:

The following individuals comprised the working-group sub-committee responsible for producing this position paper. All listed provided ideas and intellectual content, and helped shape the final form of this manuscript. Asterisk denotes additional responsibility for the primary writing of substantial portions of the document.

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The Working Group on Image-Guided Tumor Ablation is an international consortium comprised of likeminded radiologists who share an interest in investigating and exploring the potential uses of image-guided tumor ablation therapies. The working group is currently organized and co-chaired by J. William Charboneau (Rochester, MN), Luigi Solbiati (Busto Arsizio, Italy), and Damian E. Dupuy (Providence, RI), and administered by William N. McMullen (Boston, MA).

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