SPECIAL COMMUNICATION

Image-Guided Biopsy in the Era of Personalized Cancer Care: Proceedings from the Society of Interventional Radiology Research Consensus Panel

Alda L. Tam, MD, Howard J. Lim, MD, Ignacio I. Wistuba, MD, Anobel Tamrazi, MD, PhD, Michael D. Kuo, MD, Etay Ziv, MD, PhD, Stephen Wong, PhD, Albert J. Shih, PhD, Robert J. Webster, III, PhD, Gregory S. Fischer, PhD, Sunitha Nagrath, PhD, Suzanne E. Davis, MMS, MBA, Sarah B. White, MD, and Kamran Ahrar, MD

ABBREVIATIONS

CTC = circulating tumor cell, ctDNA = circulating tumor DNA, EM = electromagnetic, FDA = Food and Drug Administration, FDG = [^{18}F]fluorodeoxyglucose, FFPE = formalin-fixed, paraffin-embedded, FNA = fine needle aspiration, NGS = next-generation sequencing, PET = positron emission tomography, RCP = research consensus panel

From the Departments of Interventional Radiology (A.L.T., K.A.) and Translational Molecular Pathology (I.I.W.) and Division of Cancer Medicine, Research Planning and Development (S.E.D.), University of Texas M.D. Anderson Cancer Center; and Department of Systems Medicine & Bioengineering, Houston Methodist Research Institute (S.W.), Houston, Texas; Division of Vascular and Interventional Radiology (A.T.), Johns Hopkins University School of Medicine, Baltimore, Maryland; Department of Radiological Sciences (M.D. K.), David Geffen School of Medicine at UCLA, Los Angeles, California; Departments of Interventional Radiology and Computational Biology (E.Z.), Memorial Sloan–Kettering Cancer Center, New York, New York; Departments of Radiology, Neuroscience, Pathology & Laboratory Medicine, Weill Cornell Medical College of Cornell University (S.W.), New York, New York; Departments of Mechanical and Biomechanical Engineering (A.J.S.) and Chemical and Biomedical Engineering (S.N.), University of Michigan, Ann Arbor, Michigan; Department of Mechanical Engineering (R.J.W.), Vanderbilt University, Nashville, Tennessee; Automation and Interventional Medicine Robotics Lab, Department of Mechanical Engineering (G.S.F.), Worcester Polytechnic Institute, Worcester, Massachusetts; and Division of Vascular and Interventional Radiology (S.B.W.), Medical College of Wisconsin, Milwaukee, Wisconsin; and Division of Medical Oncology (H.J.L.), University of British Columbia, British Columbia Cancer Agency, Vancouver, British Columbia, Canada. Received October 21, 2015; final revision received and accepted October 23, 2015. **Address correspondence to** A.L.T., Department of Interventional Radiology, Unit 1471, University of Texas M.D. Anderson Cancer Center, PO Box 301402, Houston, TX 77230-1402; E-mail: alda.tam@mdanderson.org

Grant support for this work was received from the SIR Foundation. A.L.T. received grants from AngioDynamics (Latham, New York). S.W. has a related patent pending (US 2012/0022367 A1). G.S.F. received grants from the National Institutes of Health and is a paid consultant for Centauri Surgical Systems (Durham, North Carolina). G.S.F. has patents pending for apparatus and methods for magnetic resonance imaging–compatible hepatic interface, system and method for robotic surgical intervention, and a system and method for underactuated control of insertion path for asymmetric-tip needles. S.B.W. received a Radiological Society of North America Scholar Grant and grants from Guerbet (Roissy, France) and Siemens (Erlangen, Germany). None of the other authors have identified a conflict of interest.

J Vasc Interv Radiol 2015; XX:■■■–■■■

http://dx.doi.org/10.1016/j.jvir.2015.10.019

BACKGROUND

Image-guided percutaneous biopsy is a common procedure in oncology that is integral in confirming the diagnosis of cancer, staging the disease, and determining tumor histology. However, in the era of personalized medicine, in which advances in knowledge of specific cellular pathways and characterization of tissue at molecular and genetic levels has resulted in an increase in targeted therapies, the role of the image-guided percutaneous biopsy is evolving (1). Biopsy samples are required for more than just histologic diagnosis, as biomarker status now guides standard-of-care therapy in a growing number of solid tumors including melanoma, breast, colon, and lung cancers. In addition, biopsies are no longer being performed only at the time of initial diagnosis, but are being performed at multiple time points to detect progression, predict prognosis, and guide next-line therapy (1). Image-guided biopsies are also playing an increasing role in oncologic clinical trials (2,3), as the US Food and Drug Administration (FDA) has mandated that targeted therapies be accompanied by a companion diagnostic test for appropriate patient selection (4). The research biopsy is so critical to clinical trial design that many stakeholders share the sentiment that the absence of high-quality biologic specimens is one of the most significant roadblocks to developing and validating biomarkers for their intended use (5,6). Finally, prioritizing the actualization of personalized cancer care in the United States was brought to the forefront by President Obama in his 2015 State of

the Union address, in which he announced the Precision Medicine Initiative, which should "bring us closer to curing diseases like cancer."

Because biologic specimens acquired from biopsies will continue to play an important role in this era of cancer medicine, and the majority of biopsies are now being performed by radiologists with the use of image guidance (7), the Society of Interventional Radiology (SIR) Foundation gathered a multidisciplinary group of experts to form a research consensus panel (RCP) to explore how image-guided biopsy should evolve to meet the future needs of patients.

METHODS

Panel Membership

On June 1, 2015, the SIR Foundation assembled an RCP meeting for the development of a research agenda on image-guided biopsy in the era of personalized medicine. The panel membership included (*i*) a multidisciplinary group of expert panelists, (*ii*) representatives from governmental agencies, and (*iii*) representatives from industry. There were 11 expert panelists, including three interventional radiologists, one medical oncologist, one molecular pathologist, four biomedical and/or mechanical engineers, one chemical engineer, and the executive director of clinical research for cancer medicine at a National Cancer Institute designated cancer center. Representatives from the FDA Laboratory of Cardiovascular and Interventional Therapeutics and the Molecular Pathology and Cytology Branch were also present. Industry representatives came from major pharmaceutical companies, medical device companies, and manufacturers of medical imaging equipment. A member from the SIR Comparative Effectiveness Committee was also present.

Agenda Methodology

The goals of the RCP were to (*i*) provide a summary of the key aspects of the existing knowledge base, (*ii*) identify gaps in current knowledge, and (*iii*) provide and prioritize research recommendations. In addition, the panelists were asked to identify critical alliances that should be developed to advance the prioritized research and determine how the SIR Foundation could support these initiatives.

Ten panelists were asked to give a focused (10-minute) presentation in his or her area of expertise. Specifically, panelists were asked to (*i*) define the most important clinical questions that could realistically be answered through pivotal multiinstitutional clinical trials or registries, (*ii*) describe the most promising future directions that merit preclinical or early clinical exploration, and (*iii*) outline how SIR investigators could engage in these initiatives. The critical question was how to obtain high-quality biopsy tissue samples that could be processed for a number of pathologic assessments from a percutaneous image-guided approach. As such, the topics for the RCP largely revolved around the current status and potential future directions for target identification, localization, and verification.

Following the presentations, a round-robin discussion was held to identify gaps in knowledge, examine important research questions, explore potential opportunities for future research studies, and consolidate similar ideas into a short list of potential research topics. Thereafter, comments were invited from the audience. Finally, the preclinical and clinical research ideas were prioritized.

RESULTS

The panel produced 10 presentations, the results of which are summarized as follows.

Why Biopsies Are Critical

Carcinogenesis is an immensely complex process, such that, even within a histologic cancer subtype—for example, adenocarcinoma of the lung or breast—there is significant variability in cancer behavior and response to therapy. The identification of an oncogene, or other specific products required by the tumor cells for sustained growth, followed by administration of a specific inhibitor to the target, are the basis of personalized cancer treatment. Frequently, multiple different signaling pathways are involved in disease growth and progression. The pathways involved can change over the course of the disease, creating mutational heterogeneity and resulting in significant challenges for therapy. Intratumoral heterogeneity occurs when the dominant cellular composition and/or gene expression varies within the tumor at a specific site of disease within one person. In a study by Gerlinger et al (8), multiple biopsy samples were taken from patients with metastatic renal-cell carcinoma for the purposes of whole-exome sequencing as part of a predictive clinical trial with everolimus. Significant variations of gene expression and prognostic signatures were found within biopsy samples within the same tumor (8). Temporal tumoral heterogeneity can also result in genomic variations within the same and/or metastatic tumors over time. For example, it is known that breast cancer biomarkers, such as estrogen, progesterone, and HER2 receptors, vary by 32.4% when biopsies of the primary tissue are compared with biopsies of relapsed metastatic tissue (9). Therefore, biopsies of biologically relevant tissue, adequate for the evaluation of the genetic signature encoded in DNA and RNA, are essential for the analyses needed to determine and develop future treatments.

Currently, the method of acquisition of tissue can be variable and lacks standardization, ranging from different sampling techniques [fine needle aspiration (FNA) vs core biopsy] to different sampling sites (primary vs