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Keynote Addresses

Translational molecular imaging for oncology

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Although most clinical diagnostic imaging studies employ anatomic techniques such as CT and MRI, much of radiology research currently focuses on adapting these conventional methods to physiologic imaging, as well as introducing new techniques and probes for molecular imaging – studying processes at the cellular and molecular levels *in vivo*. Molecular imaging promises to provide new methods for early detection of disease and support for personalized therapy. Although molecular imaging has been practiced in various incarnations for more than 20 years in the context of nuclear medicine, other imaging modalities have only recently been applied to the noninvasive assessment of physiology and molecular events. Nevertheless, we have sufficient experience with specifically targeted contrast agents and high-resolution techniques for MR imaging and other modalities to begin moving these new technologies from the laboratory to the clinic. This brief overview outlines molecular imaging from probe development to clinical translation, with a focus on translational (small animal) and early clinical imaging; for instance, molecular imaging can assess specific signal transduction cascades, which are increasingly the targets of newer, cytostatic therapeutic agents, and provide examples of how existing or readily accessible molecular tracers and techniques provide insight into complex biological phenomena *in vivo*.

Complexities in imaging the ovary

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Ovarian cancer is the most frequent cause of death from gynecologic cancers in the United Sates. Most patients present with advanced stage disease, which while responsive to chemotherapy is essentially incurable. Thus, an accurate noninvasive evaluation of the ovary is critical for screening, diagnosing, and monitoring ovarian cancer. Present imaging modalities include transabdominal ultrasound, transvaginal ultrasound, Doppler imaging, and CT, MRI, and PET scanning. The effectiveness of these modalities are highly dependent upon the specific clinical question being addressed.

No imaging technique or combinations of techniques has proven to be successful for screening. In general, transabdominal ultrasound is reasonably sensitive and specific. Transvaginal ultrasound, which brings the probe closer to its target, has increased sensitivity and specificity, and Doppler imaging adds additional specificity. However, given the low prevalence of this disease, positive predictive rates using these techniques are unacceptably low. In addition, combinations of these techniques do not provide sufficient accuracy to be useful for screening.

Diagnostic imaging of the ovary utilizes the same techniques as screening. Most studies demonstrate that transvaginal ultrasound is the procedure of choice due to its sensitivity and specificity. The ability to visualize complexities within the cyst/mass provides additional accuracy. In addition, MRI with contrast of identified masses adds additional specificity. However, regardless of imaging, the procedure of choice for most ovarian masses is laparoscopy or laparotomy-guided biopsy.

Future directions will most certainly involve new technologies, which can specifically identify early molecular events occurring on ovarian epithelium during its transformation. Mutations within oncogenes,

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signaling pathways, or cell surface proteins would serve as appropriate markers. It remains critical that we specifically detail these molecular changes and develop the methods to image them.

Pancreatic cancer and imaging

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Pancreatic cancer's occult nature and late-stage presentation, lack of early symptoms and reliable systemic biomarkers, early invasion and metastasis, and chemoresistance, result in advanced or unresectable disease for over 80% of patients. In this population, the cure rate is only 4–5%, and a median survival without treatment is only about three months. Potential screening strategies involve epidemiologic associations such as smoking, diabetes, and obesity, and genetic factors such as hereditary pancreatitis, BRCA2, HNPCC, and Li Fraumeni syndrome. Significant advances in understanding the molecular pathogenesis of pancreatic cancer have led to a proposed pancreatic intraepithelial neoplastic (PanIN) precursor. Various oncogene activation or overexpression events (e.g., K-ras, epidermal growth factor receptor), tumor suppressor pathway mutations or derangements (p53, p16, SMAD), and other pancreatic carcinogenic processes (angiogenesis, adhesion molecule and inflammatory changes, etc.) provide opportunities to apply these discoveries to improve early detection and treatment. Endoscopic imaging with ultrasound and endoscopic retrograde cholangiopancreatic duct collection of cells and fluid might be combined with better immunocytochemical, microarray, or proteomic profiling of preneoplastic tumor stages. The hypoxic microenvironment of pancreatic cancer also suggests ways to develop imaging probes, while new and better animal models provide test environments to evaluate rationally designed diagnostic and treatment candidates for pancreatic cancer.