Emerging Molecular Imaging Techniques in Gynecologic Oncology

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KEYWORDS

• Cervical cancer • Endometrial cancer • Ovarian cancer • Vulvar cancer • MR imaging • Molecular imaging • PET • Radiomics

KEY POINTS

- Molecular imaging has played important roles in tumor detection, primary staging, treatment planning, prediction of prognosis, response evaluation, surveillance, and management of recurrence.
- Emerging MR imaging–based technologies include diffusion-weighted imaging, chemical exchange saturation transfer imaging, dynamic contrast enhancement–MR imaging, and magnetic resonance spectroscopy.
- Dynamic nuclear polarization increases signal by more than 10,000-fold for stable isotope carbon-13–enriched compounds on MR imaging.
- ^{18}F-fluorodeoxyglucose–PET provides semiquantitative functional readouts: standardized uptake value maximum, total lesion glycolysis, and metabolic tumor volume.
- Radiomics converts high-throughput extraction of quantitative imaging features into mineable data by machine-learning tools and will evolve rapidly for decision support in the near future.

INTRODUCTION

Molecular imaging in oncology refers to in vivo spatial and temporal analysis of the key biomolecules representing the cancer phenotype. Tumor heterogeneity is not only attributed to genetic alteration but also an adaptation to the tumor microenvironment. The anatomy of the female pelvis contains delicate structures, and many oncologic lesions are better demonstrated using molecular imaging tools. The most prominent example, the Warburg effect, explains how glycolysis confers a significant growth advantage by producing lactate as oxidative fuel, sparing glucose for the more anoxic cells in the center of the tumor.[1] Because tumor heterogeneity and its adaptations to microenvironment are important factors that could affect the effectiveness of cancer treatment, the ability to image and spatially map the heterogeneity of metabolism within a tumor will be beneficial for planning the treatment regime in gynecologic oncology.[2]

Advances in MR imaging techniques have enabled noninvasive assessment of structural,

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functional, and metabolic phenotypes of cancer on a variety of scales. The complex relaxation mechanisms of nuclear spins provide unique and convertible tissue contrasts, offering abundant parameters that can be extracted from a single acquisition to provide general structural data, functional pathophysiologic data, and various heterogeneity-based metrics in the tumor. Moreover, it is critical to understand each data acquisition and reconstruction scheme for proper image analysis and valid assessment of associated metabolic parameters. The most prominent applications include diffusion-weighted imaging (DWI),[3] chemical exchange saturation transfer (CEST) imaging,[4] dynamic contrast enhancement (DCE)–MR imaging,[5] and magnetic resonance spectroscopy (MRS).[6] The latest addition to the MR imaging armamentarium is the dynamic nuclear polarization (DNP), which could increase signal more than 10,000-fold for stable isotope carbon-13 (^{13}C) -enriched compounds.[7] These imaging modalities could provide markers for tumor diagnosis, prognosis, and treatment response, as well as insights into cancer biology and factors that promote tumor growth.

PET detects pairs of gamma rays emitted indirectly by specifically labeled radionuclide tracers, to provide functional or metabolic information in various disease scenarios.[2] ^{18}F-fluorodeoxyglucose (FDG) PET is by far the most widely used imaging technique to study glucose uptake in tumors in vivo. The semiquantitative imaging parameters of the tumor, for example, standardized uptake value maximum (SUV_{max}), total lesion glycolysis (TLG), and metabolic tumor volume (MTV), are used in daily oncology practice.[2] In addition to FDG, ^{11}C-choline[8] and 3′-deoxy-3′-^{18}F-fluorothymidine (FLT)[9] have been used to assess the diagnosis and treatment response in patients with cancer, with many other PET radiotracers under development on the pipeline.

A novel analysis approach, radiomics, refers to the extraction and analysis of large amounts of quantitative imaging features with high throughput from computed tomography (CT), PET, or MR imaging.[10] Radiomics data are mineable information that can be used to build descriptive and predictive models relating image phenotypes and to provide valuable diagnostic, prognostic, or predictive information.[10]

The purpose of this review is to summarize the literature pertaining to emerging techniques in MR imaging and PET, as well as new radiomics analyses, that hold translatable potential for gynecologic oncology in the clinic.

MR IMAGING

Diffusion-Weighted Imaging Measurements Reflecting Tumor Microstructure

DWI is an MR imaging method that is sensitive to the Brownian motion of water molecules. Because most cancer types demonstrate an increased cellularity than the adjacent normal tissue, tumors are highlighted on DWI and can be measured quantitatively on the apparent diffusion coefficient (ADC) map. Newer DWI techniques, such as computed DWI resulting in higher b values, could potentially increase diagnostic specificity by improving the suppression of signal from normal tissues that may mimic disease.[3] The ADC values may provide additional information about tumor microstructure with potential relevance for staging and prediction of aggressive disease. For example, low ADC values of endometrial cancers are associated with deep myometrial invasion, cervical involvement, and lymph node metastases, and in patients with high-grade endometrioid subtype.[11] Furthermore, ADC minimum significantly predicts a reduced disease-free survival,[11] suggesting that tumor ADC measurements may potentially aid in risk stratification when selecting patients for treatment. Whole-body DWI for the staging of patients with suspected ovarian cancer was reported superior to CT or F18-FDG/CT, with a 94% accuracy rate for primary tumor characterization and 91% accuracy for peritoneal staging.[12]

Chemical Exchange Saturation Transfer Imaging

CEST imaging selectively saturates exogenous or endogenous compounds containing either exchangeable protons or molecules, detected indirectly through the water signal with enhanced sensitivity.[4] The extracellular pH (pH_e) decrease correlates with tumor proliferation, invasion, metastasis, and chemoresistance, which can be detected by CEST. CEST MR imaging has been used to achieve pH_e mapping of the cancer microenvironment by in vitro studies on hepatoma cell lines and in vivo in an MMTV-Erbb2 transgenic mouse breast cancer model.[13] CEST imaging was capable of differentiating radiation necrosis from tumor progression in brain metastases, superior to the conventional amide proton transfer imaging.[14] An emerging technique, acidoCEST-MR imaging, uses an exogenous compound, iopromide, to assess in vivo pH_e more accurately as compared with ^{31}P MRS.[15] Because of its sensitivity to motion artifact, there has not yet been application of this technique in gynecology oncology.