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MODERN PATHOLOGY

A weighted-risk model of uterine leiomyosarcoma

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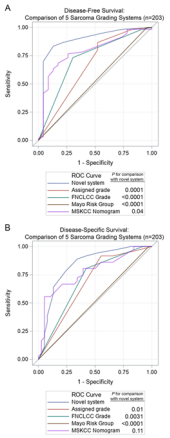

Uterine leiomyosarcoma most often presents at stage I, but these uterus-confined tumors have varied prognoses. A subset are cured by surgery, but 50–70% recur, often fatally. To enhance patient-specific prognostication, Chapel et al. sought to better define the morphologic features associated with aggressive behavior. In multivariate analyses of 203 stage I uterine leiomyosarcomas, shorter disease-free and disease-specific survival was significantly and independently associated with >25 mitoses per 2.4 mm^2 (10 high-power fields), atypical mitoses, coagulative necrosis, lymphovascular invasion, and tumor directly abutting uterine serosa. These parameters were fitted to a simple weighted-risk model: risk score = (coagulative necrosis)(1) + (>25 mitoses per 2.4 mm^2)(2) + (atypical mitoses)(2) + (lymphovascular invasion)(3) + (serosal abutment)(5). The continuous risk score (range, 0–13) stratified into distinct low-risk (0–2 points), intermediate-risk (3–5 points), and high-risk (6–13 points) groups. Prospective application of this risk model will permit more precise counseling for individual patients. Risk stratification may also play a role in clinical trials pertaining to management of stage I uterine leiomyosarcoma.

Architectural distortion on mammography

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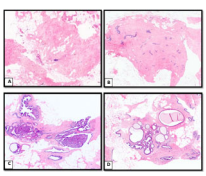

Architectural distortion (AD) on mammography is the third most common presentation of carcinoma. AD presents more challenges than masses and calcifications because the types of lesions associated with AD are less well defined and therefore what signifies a discordant finding requiring excision is less clear. Bachert et al. analyzed 588 core needle biopsies (CNBs) to evaluate the pathologic lesions associated with AD. Overall, 31% of CNBs showed invasive carcinoma or ductal carcinoma in situ (DCIS), 37% showed benign lesions likely to correlate with AD (sclerosing lesions, ruptured cysts, scarring, and fat necrosis), and 32% showed nonspecific benign findings. The invasive carcinomas tended to be low-grade (60%), ER-positive (98%), and HER2 negative (98%), and 52% had lobular features. For CNBs with a likely correlate for AD, only 1 of 94 cases (1%) excised showed DCIS adjacent to a sclerosing lesion. However, for the CNBs without a correlate for AD, 6 of 68 cases (9%) showed invasive carcinoma on excision. This study shows the importance for pathologists to report benign lesions that can correlate with AD as excision may be unnecessary for these patients.

LABORATORY INVESTIGATION

Novel cell lines of rare sarcomas for exploring new therapeutics

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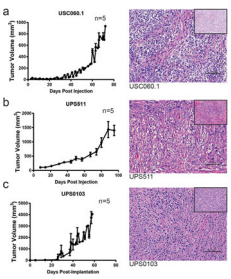

Achieving a better understanding of tumors with limited cell-line availability is challenging. Bhalla et al. studied two rare cancers—undifferentiated pleomorphic sarcoma and malignant peripheral nerve sheath tumor—both aggressive soft-tissue sarcomas with limited effective treatment options. The group generated a series of patient-derived cell lines and validated them by assessing their tumorigenic potential in vitro and in vivo. They established xenografts via subcutaneous injection into immunocompromised mice and determined the repassaging potential of the cell lines, which were still going at 1–2 years at the time of publication. The group also confirmed that mouse cells were not contaminated by the xenografts and that the short tandem repeat profiles matched those of the originating cancer types. The new cell lines will be useful for detailed tumorigenesis studies of the two tumor types as well as investigations into novel therapeutics for them.

An AI-based IHC technique for assessing target proteins

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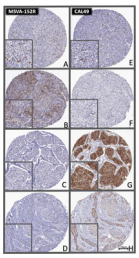

Dum et al. performed a comparative analysis of CTLA-4^{+} cells of tumor entities using a sample of 4,582 tumor samples from 90 tumor entities as well as 608 samples from 76 normal tissue types and analyzing them by immunohistochemistry on a tissue microarray. The group validated and compared two CTLA-4 antibodies and assessed nonspecific staining differentials, which enabled them to eliminate the nonspecific staining pattern. High CTLA-4^{+} cell density and a high CLTA-4/CD3 ratio were linked to absent lymph node metastases and PD-L1 expression in tumor and inflammatory cells. Different tumor types varied markedly in the number of CTLA-4^{+} lymphocytes. This approach of using two different antibody clones with different staining patterns and applying a machine learning algorithm facilitated automated scoring of the marker across a variety of tumor types.

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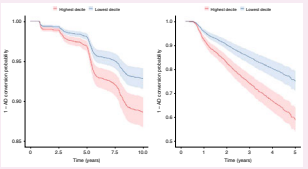
Validation of novel genetic risk factors for Alzheimer's disease

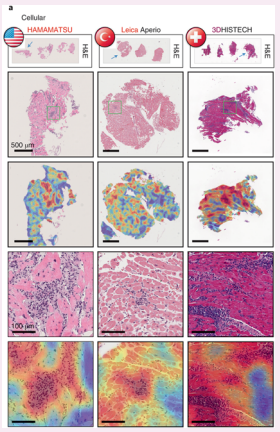
Exploring the genetic landscape of Alzheimer's disease (AD) and related dementias (ADD) will enhance understanding of the pathophysiological processes involved. Bellenguez et al. performed two-stage genome-wide association studies of over 111,000 clinically diagnosed patients and just under 700,000 controls. They found 75 risk loci, 42 of which were new. Of those identified, 31 genes were suggestive of new genetically associated processes and as such enabled the group to build out a new genetic risk score indicative of the chances of future AD/dementia. They validated 33 previously identified loci and doubled the total number of genetic loci associated with risk of ADD. The authors propose that the new targets may lead to development of novel therapeutics and personalized medicine.



Nature Genetics 2022;54:412–436; https://doi.org/10.1038/s41588-022-01024-z

An artificial intelligence tool for improving heart transplant outcomes

Lipkova et al. developed a deep learning–based artificial intelligence (AI) system named the Cardiac Rejection Assessment Neural Estimator (CRANE). It can assess gigapixel whole-slide images obtained from endomyocardial biopsies, the interpretation of which is the standard of care for detecting allograft rejection. Inter- and intraobserver variability can lead to inappropriate follow-up (unnecessary additional biopsies, inappropriate therapies, and poor transplant outcomes). To optimize the system, a dataset from the United States was curated, along with test cohorts from Turkey and Switzerland (to introduce variability of population, sample preparation, and equipment). The team proposes that the use of CRANE as an assistive diagnostic tool will decrease interobserver variability, improve robustness and accuracy of rejection assessment, and screen for cases that might be time-sensitive and benefit from priority inspections. Tying in molecular biomarkers could increase functionality and enable this AI-based assessment to improve heart transplant outcomes.



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