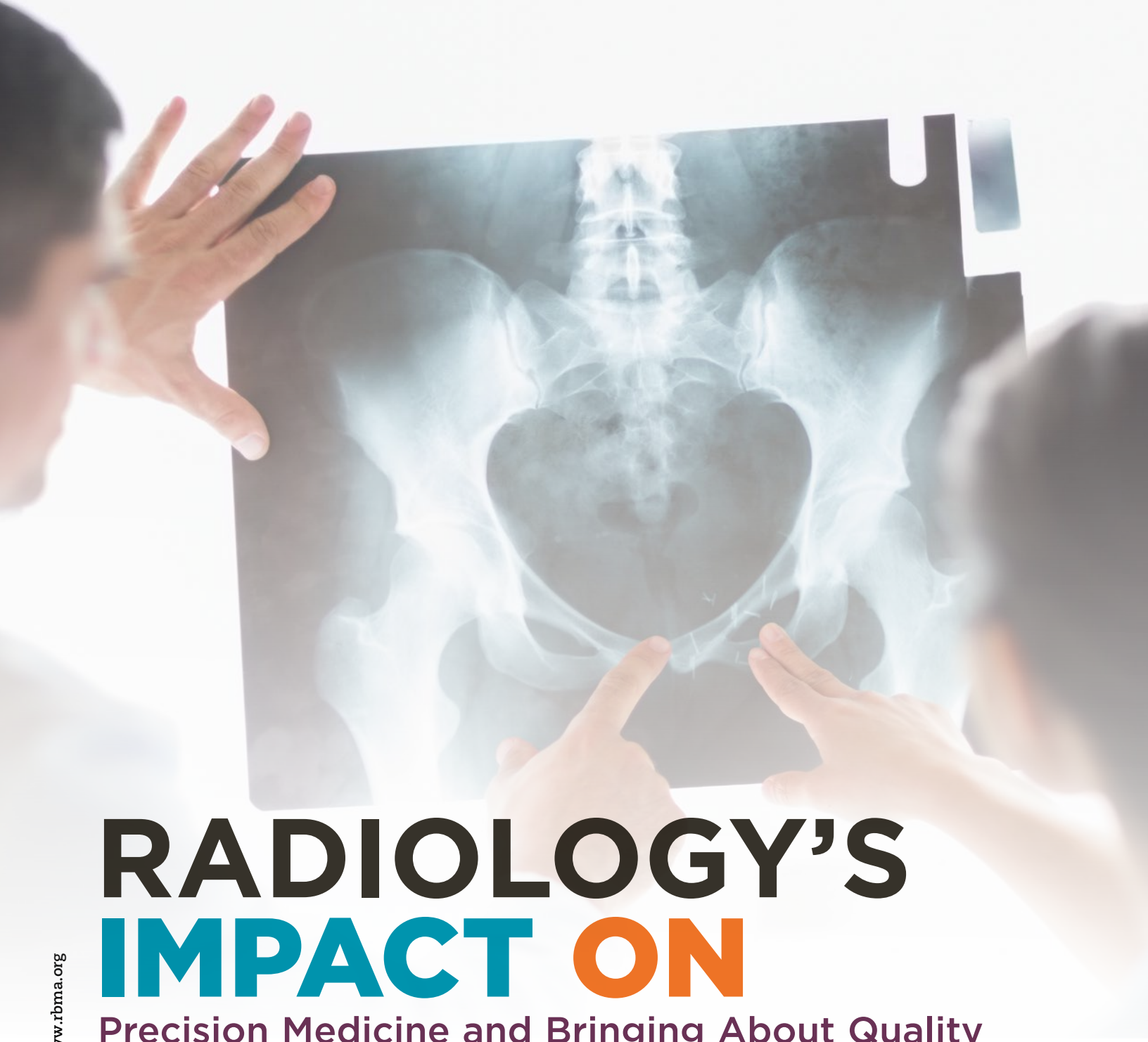


RADIOLOGY'S IMPACT ON

Precision Medicine and Bringing About Quality

BY DAVID BYRD

Experience has shown that breakthroughs in the diagnostic sector of healthcare can heavily influence patient wellness and patient care plans. Today, we are experiencing these breakthroughs more quickly and with greater impact than ever before. Many of these advancements are based upon procedures that are performed by diagnostic physicians combined with cutting-edge, proprietary lab tests that center on the human genome.

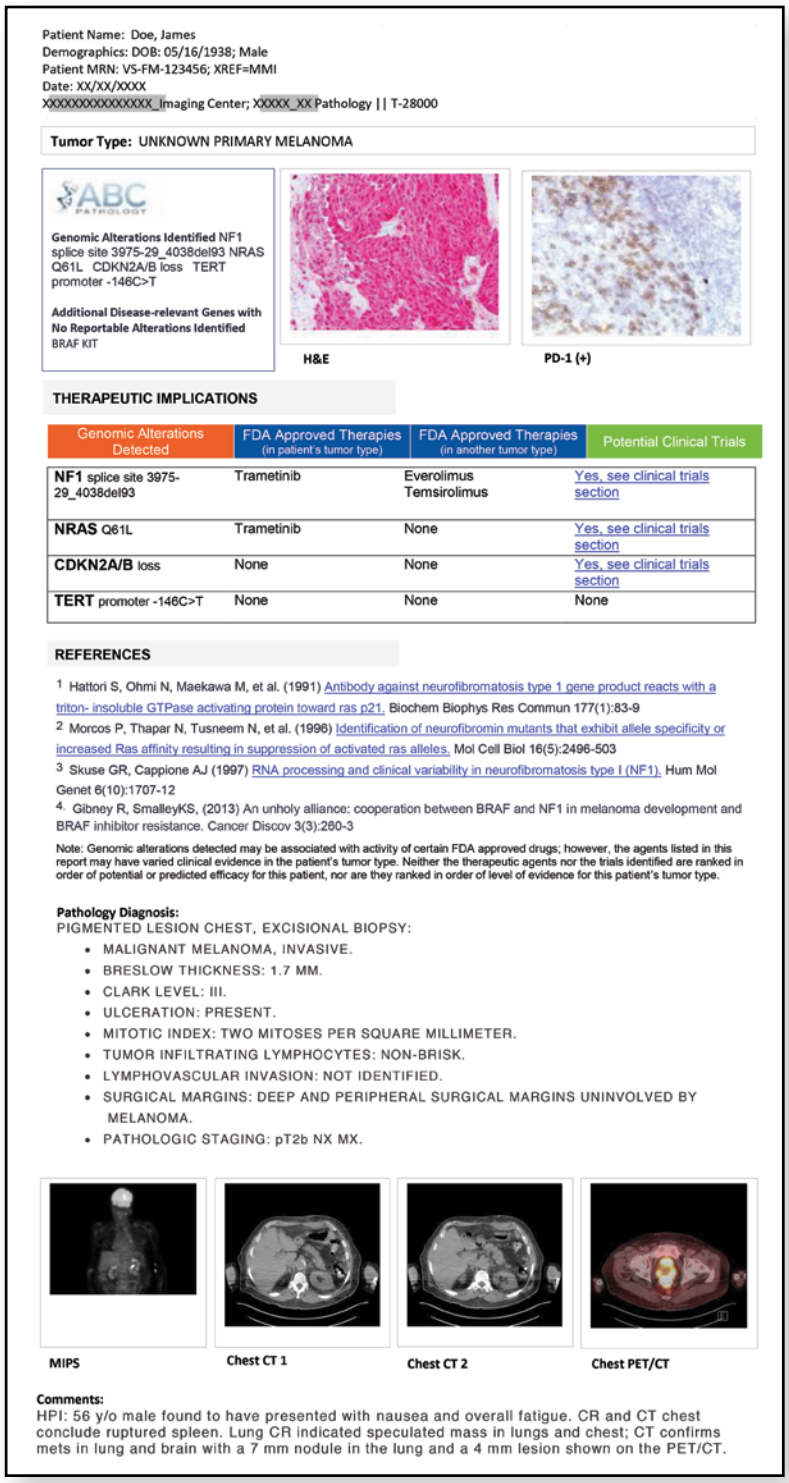
More and more attention is being paid to the activities around precision medicine and how the protocol will bring about more focused care plans for both healthy and sick patients. The objective of precision medicine is to provide the right treatment at the right time. The catalyst that brought about more focus on precision medicine came in January 2015, when President Obama mentioned the term in the State of the Union address. This June, Vice President Biden followed along, talking about the "Cancer Moon-

shot" and identifying the importance of precision medicine, in an address to the attendees of the American Society of Clinical Oncology (ASCO) Conference.

Right treatment at the right time, isn't that what care providers have been doing forever?

One could make the argument they have, but not with the insight we have today and how rapidly we are starting to amass multiple data sets from different technologies on a single patient. With the advancement of Next Generation Sequencing (NGS) technologies, we can now sequence DNA and RNA much more quickly and inexpensively than before. And thus we have revolutionized the study of genomics and molecular biology. But that's just the start.

Precision medicine is for disease treatment and prevention and takes into account individual variability in genes, environment, and lifestyle for each person, but from the perspective of a cohort or a group of individuals who share a characteristic at some specific time, and who are then followed forward in time, with data being collected at one or more suitable intervals. This is why the U.S. government placed $215 million dollars into the PMI Cohort Program. This program is a participant-engaged, data-driven enterprise supporting research at the intersection of human biology, behavior, genetics, environment, data science, computation, imaging, and much more to produce new knowledge with the goal of developing more effective ways to prolong health and treat disease.



Patient Name: Doe, James
Demographics: DOB: 05/16/1938; Male
Patient MRN: VS-FM-123456; XREF=MMI
Date: XX/XX/XXXX
XXXXXXXXXXXXXX_Imaging Center; XXXXX_XX Pathology || T-28000

Tumor Type: UNKNOWN PRIMARY MELANOMA

ABC PATHOLOGY

Genomic Alterations Identified NF1 splice site 3975-29_4038del93 NRAS Q61L CDKN2A/B loss TERT promoter -146C>T

Additional Disease-relevant Genes with No Reportable Alterations Identified
BRAF KIT

H&E PD-1 (+)

THERAPEUTIC IMPLICATIONS

Genomic Alterations Detected	FDA Approved Therapies (in patient's tumor type)	FDA Approved Therapies (in another tumor type)	Potential Clinical Trials
NF1 splice site 3975-29_4038del93	Trametinib	Everolimus Temsirolimus	Yes, see clinical trials section
NRAS Q61L	Trametinib	None	Yes, see clinical trials section
CDKN2A/B loss	None	None	Yes, see clinical trials section
TERT promoter -146C>T	None	None	None

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2 Morcos P, Thapar N, Tusneem N, et al. (1996) Identification of neurofibromin mutants that exhibit allele specificity or increased Ras affinity resulting in suppression of activated ras alleles. Mol Cell Biol 16(5):2496-503
3 Skuse GR, Cappione AJ (1997) RNA processing and clinical variability in neurofibromatosis type I (NF1). Hum Mol Genet 6(10):1707-12
4 Gibney R, SmalleyKS, (2013) An unholy alliance: cooperation between BRAF and NF1 in melanoma development and BRAF inhibitor resistance. Cancer Discov 3(3):260-3

Note: Genomic alterations detected may be associated with activity of certain FDA approved drugs; however, the agents listed in this report may have varied clinical evidence in the patient's tumor type. Neither the therapeutic agents nor the trials identified are ranked in order of potential or predicted efficacy for this patient, nor are they ranked in order of level of evidence for this patient's tumor type.

Pathology Diagnosis:
PIGMENTED LESION CHEST, EXCISIONAL BIOPSY:

- MALIGNANT MELANOMA, INVASIVE.
- BRESLOW THICKNESS: 1.7 MM.
- CLARK LEVEL: III.
- ULCERATION: PRESENT.
- MITOTIC INDEX: TWO MITOSES PER SQUARE MILLIMETER.
- TUMOR INFILTRATING LYMPHOCYTES: NON-BRISK.
- LYMPHOVASCULAR INVASION: NOT IDENTIFIED.
- SURGICAL MARGINS: DEEP AND PERIPHERAL SURGICAL MARGINS UNINVOLVED BY MELANOMA.
- PATHOLOGIC STAGING: pT2b NX MX.

MIPS Chest CT 1 Chest CT 2 Chest PET/CT

Comments:
HPI: 56 y/o male found to have presented with nausea and overall fatigue. CR and CT chest conclude ruptured spleen. Lung CR indicated speculated mass in lungs and chest; CT confirms mets in lung and brain with a 7 mm nodule in the lung and a 4 mm lesion shown on the PET/CT.

So what does this have to do with imaging and quality?

Combining the genotype with the phenotype is where radiology comes into play, especially when it comes to cancer. First let's make sure we are on the same page addressing the words genotype and phenotype. The genotype is the set of genes in our DNA that is responsible for a particular trait. Importantly, a genotype cannot be observed; it can only be determined through a biological lab test. The genotype contains "alleles," which are a series of genes on a chromosome that contain heredarity traits that result in some of the physical traits of an organism, such as eye and hair color. Phenotype is where imaging starts to come in—it's the actual gene result that we observe combined with the environmental influence on an organism's appearance or behavior. So in some cases, a radiology study could be viewed as a phenotype description identifying the finding via the image and report.

As with many medical cases, correct patient care cannot happen without a radiology procedure, and cancer is a perfect example. As we know, cancer is a complex disease that begins when abnormal cells in any part of the body start to grow out of control, forming tumors that behave almost like new organs with their own immune cells and blood vessels. While growing, tumors can make themselves hidden to the body by stopping immune responses that would have been directed against them. In many cancers and other serious illnesses, signs and symptoms of the disease often do not become apparent until the illness reaches an advanced and more difficult stage.

Diagnostic imaging's medical value has grown in importance with advances in technology like computed tomography (CT), ultrasound, magnetic resonance imaging (MRI), positron emission tomography (PET), and the obvious emerging technology, molecular imaging. Additionally, advancements in digital pathology imaging are gaining traction within the medical community, shaping the way for FDA approval for pathologists to perform primary reads for diagnosis through digital pathology imaging, versus a glass slide. The impact of combining NGS testing (genotype) with imaging (phenotype) is the next big leap in diagnostics and why the cancer moonshot is within reach.

We are now seeing many university medical centers within the U.S. leading the way in precision medicine to align with quality measures and value-based pricing by tearing down the silos between molecular lab, pathology, radiology, and oncology departments in their approach to create specific care plans based upon the patient's genomic make-up and their phenotype. Radiology is absolutely vital in this process and takes a key role in molecular tumor boards or multi-disciplinary teams, as observation of a tumor size can only be seen through a radiology image identifying whether the care plan is effective or not, is the tumor growing or is it shrinking.

The technologies being acquired, such as NGS sequencers, pathology slide scanners (think of a copier machine that is for pathology glass slides), and digital pathology imaging "cockpits" that provide the radiology image for a side-by-side comparison view with clinical content, are now being leveraged. Tearing down the data silos is important for quality measure reporting and reimbursement/value-based pricing.

For example, melanoma is reported through PQRS 397, continuity of care and coordination of care addressed through PQRS 137 and 138, as well as overutilization or imaging through measure 224, and follow-up of a biopsy through measure 265. CPT codes in this scenario address radiology 71260 CT/ 70460 CT, pathology 88307/88308 surg, 88331 mRNA, 81540, BRAF 81210, solid tumor 81445, and CPT codes 00366, 99367, and 99368 for multi-disciplinary team efforts.

It is important to note the consolidations of data that radiologists, pathologists, and oncologists are using to address precision medicine is being utilized in a summarized consolidated report for reference and distribution purposes. These reports can be configured to contain clinical notes, ad-hoc notes from multi-disciplinary team meetings, image annotations, billing codes, quality measure codes, etc.

As equally important, precision medicine ascribes to the idea that patients are to be involved in their own care and certain quality measures are slowly starting to push this initiative through indirect measures addressing surveys, follow-up visits and patient engagement. Providing patient data in a consolidated report for use between physicians has always been a goal since the advent of the EMR/EHR, but providing clinical data to patients for their understanding and reference is also taking place for follow-up purposes to referring physicians, as well as for second opinions.

Technology being used today by leading institutions allows for the consolidation of key diagnostic images, both radiology and pathology with molecular and oncology content in a standardized care report that can then be ingested into an EMR/EHR in a Continuity of Care Document (CCD) format or provided to the patient in a PDF format for review or to provide for a second opinion. As patients start to gain exposure to the diagnostic environment, through such interaction with a consolidated report, radiologists and radiology administrators have a real opportunity to identify the importance of radiology in precision medicine and actually engage with the patient, assisting in patient satisfaction, which is part of the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) quality measure.

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is vice president of business development, XIFIN Inc., and provider of cloud-based revenue cycle management solutions. David has nearly two decades of healthcare information, technology-related, and business development experience. He has been a longstanding member of the RBMA and Healthcare Information Management Systems Society. He can be reached at (858) 793-5700 or dbyrd@XIFIN.com.