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Improving Genomic Coding for Plasma-Based Comprehensive Genomic Profiling

In this paper, we review the specialized world of genomic test coding, how it develops, and where it's going next. We focus on the rapidly adopted use cases for liquid biopsy in cancer management, and show why new coding is needed.

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Overview

The clinical utility of comprehensive genomic profiling in cancer is increasingly well-recognized, across the clinical literature, in updated guidelines (Imai et al. 2022; Pascual et al. 2022), and in Medicare coverage policies (Foundation_Medicine 2015; CMS 2021; NGS_MAC 2022; PalmettoGBA_MAC 2022). One driver for the use of larger and comprehensive panels is the need to measure tumor mutational burden, which has been discussed in a 2022 white paper (Quinn 2022).

Comprehensive genomic profiling (CGP) can now be accomplished with plasma-based testing, rather than formalin-fixed paraffin-embedded (FFPE) tissue testing. This newer technology meets several important needs for some cancer patients:

- Plasma-based CGP is available in cases when solid tumor tissue is not available or accessible, avoids potential hazards of invasive biopsies, and avoids biopsy costs.
- Plasma-based testing can be performed serially, such as following a clinical relapse, to determine the molecular causes of therapy resistance.
- Plasma-based testing concurrently samples from all tumor sites in patients with metastatic cancer, overcoming sampling bias. This is a limitation of tumor sampling from a single biopsy (which cannot sample a tumor's full heterogeneity), and plasma biopsy may improve the therapy selection process.

Policies for coding and payment in genomics usually lag clinical practice improvements, and that is the case for plasma-based CGP.

1.1 Lags in Coding:

The standard AMA code set for genomics doesn't distinguish between specimen sources (tissue, plasma, etc.). However, the PLA code set, whose rules and conventions are much newer, allows precise definition of the specimen source, and labs have been able to code their services with increased specificity. There are already a number of PLA codes specific to plasma-based tumor testing and this number is steadily increasing. We show why it has become important to create Category I AMA codes for plasma-based testing.

1.2 Reimbursement:

Plasma-based testing also affects appropriate reimbursement, but this requires codes that specify plasma-based testing as the underlying technology. This is exemplified by PLA codes 0239U and 0242U, which represent FDA-approved CGP tests from Foundation Medicine (FoundationOne Liquid CDx) and Guardant Health (Guardant360 CDx). CMS has set higher reimbursement rates for these plasma testing- specific codes. A key factor for this is that, while FFPE based testing of a tumor sample can be performed using Next-Generation Sequencing (NGS) in the range of 100X depth of sequencing, plasma- based testing for circulating tumor DNA – which usually accounts for less than 1% of the cell free DNA present in plasma - may require up to 10,000X depth of sequencing. In a recent study, Kramer et al. have shown that this raises the basic lab costs for plasma-based tumor testing (Kramer et al. 2023). it is important to note that plasma-based testing offers some substantial cost offsets during sample collection, compared to tissue-based testing which requires an invasive and usually image-guided biopsy. And as noted above, plasma-based CGP may be the only and most important way to get biomarker information to make clinical decisions using precision oncology.

1.3 Changes may be coming:

There has been good progress coming from the authorities for coding policy. For January 2023, AMA CPT has already introduced new target-based specificity for genomic profiling codes, with a new triplet of codes that are specific to RNA sequencing analysis in cancer, for both solid cancers and hematologic cancers. In addition, AMA CPT has also set up a workgroup with diverse expertise that has held bimonthly public meetings, to gather information on which further updates will make the coding system for cancer genomics more useful for labs, clinicians, and payors. In its public agenda for a February 2023 meeting, AMA has promised to introduce new codes “to reflect current practice in genomic sequencing.” 2023 promises to be an exciting period for policy around plasma-based CGP.

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Rapid Evolution: Comprehensive Genomic Profiling Becomes Standard of Care

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A patient's cancer should be sequenced to inform the best choice for cancer therapy. It has only been 10 years since the very first FDA approvals of single-gene tests, such as the Roche BRAF test (2011), the Qiagen KRAS test (2012),and then the QIAGEN therascreen® and Roche cobas® tests for EGFR in 2013 (FDA 2011; FDA 2023b) (FDA 2013b; FDA 2013a). From that beginning, the range and diversity of genomic tests for cancer patients has skyrocketed (FDA 2021b). FDA has now approved companion diagnostic indications for over 100 gene-drug pairs (FDA 2023a). FDA has also approved single assays with over 300 genes measured simultaneously on a single sophisticated NGS platform (e.g. the FoundationOne CDx test, (FDA 2017).

Gene-by-gene analysis with separate tests is cumbersome, slow, and costly. The new standard is "comprehensive genomic profiling," or CGP, with several factors driving this movement. First, for single cancers, there are more and more targeted therapies, each paired to a different gene or genomic feature. All of these genes with on-label therapy indications can be incorporated in a single CGP panel. Second, some newly-important genes have very low prevalence (including ALK, ROS1, and NTRK1,2,3), so testing them one at a time outside of CGP would be impractical and depletes tissue biopsy samples rapidly. Third, there are many types of oncology mutations, some of which are not easily detected by older methods. CGP tests that use next-generation sequencing report a range of different mutations in one assay, including point mutations, small and large insertion-deletions, rearrangements or oncogene fusions, and large copy number duplications and losses (Boyle et al. 2021).

A dozen cancer-specific guidelines from the National Comprehensive Cancer Network (NCCN) endorse use of CGP, as does new guidance from the American Society of Clinical Oncology (ASCO) (Chakravarty et al. 2022). The most recent publication on clinical utility of genomic testing from the Personalized Medicine Coalition (PMC) also focuses on the value of CGP (Pritchard et al. 2022). Additionally, bringing multiple genetic tests together in one assay has also been shown to be a wise choice from the viewpoint of health economics (Chawla et al. 2018; Pennell 2019; Johnston et al. 2020; Harvey et al. 2021; Patel et al. 2021).

Two more features of CGP must be noted. CGP can assess micro-satellite instability (MSI) and tumor mutation burden (TMB), both of which are important biomarkers for immune-oncology drugs (such as checkpoint inhibitors). In this area, Keytruda (pembrolizumab), was approved by the FDA in June 2020 for use in advanced solid cancers with high TMB (FDA 2020a). TMB analysis is based on sequencing of 0.7 mb or more of the tumor's DNA, as established in a recent consensus report (Vega et al. 2021). While that sequencing can be conducted as part of a whole-exome analysis, current TMB assessments are most often conducted as a part of CGP, which gives an additional and FDA-based rationale for CGP testing.

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Plasma-Based CGP: Unmet Need and New Clinical Roles

Plasma-Based CGP: Unmet Need and New Clinical Roles

The ability to detect tumor mutations (including copy number variations, rearrangements, and TMB) from plasma samples has advanced rapidly in the past five years. CGP by means of plasma-based testing, rather than paraffin block testing, meets several critically important needs for a large subset of advanced cancer patients:

- Plasma-based CGP is available in cases when solid tumor tissue is not available or accessible, avoiding potential hazards and biopsy costs. This is most frequently the case when tumors are biopsied using fine-needle aspirates, such as lung cancer, or in pediatric patients, where access to the tumor can be challenging.
- Plasma-based testing can be performed serially, such as after a clinical relapse, to determine the molecular cause of therapy resistance.
- Plasma-based testing samples concurrently from all tumor sites in patients with metastatic cancer, overcoming sampling bias from single-biopsy tumor sampling (inability to sample a tumor's full heterogeneity). A broader view of the mutation profile may improve the therapy selection process.

Under current protocols, a large proportion of patients do not receive recommended CGP – for a new study and review, see (Sadik et al. 2022). Sadik et al. studied a 500,000-patient database including both Medicare and commercially-insured patients. Half of the patients with lung cancer never received CGP testing, and some 30% of those who had biomarker results did not receive appropriate, targeted treatments. Some patients lack adequate tissue from an initial needle biopsy. Some patients may never have received a guided needle biopsy due to concerns about adverse events, which are indeed substantial, as shown most recently by Vachani and colleagues (Vachani et al. 2022).

In contrast, *every patient with advanced cancer can give a blood sample for plasma analysis.* This approach – liquid biopsy for tumor driver genes and companion diagnostics testing – is well-validated and has reached guideline endorsement both in the US and in other countries (Olsen et al. 2022; Pascual et al. 2022).

> **(In this paper, "plasma-based CGP" refers to *detection of driver genes* and newly arising mutations, and our discussion *doesn't include* other uses for plasma- based sequencing, like early detection of unknown cancers, or detection of postsurgical minimal residual disease or cancer recurrence).**

The difference between surgically-based testing and plasma testing hold even more true for serial testing. Serial tumor testing, via surgical excision or biopsy, is possible but uncommon in routine cancer care. Liquid biopsy can be performed far more easily with a high chance of providing immediately actionable biomarker information (Dietz et al. 2019; Benavides et al. 2022; Kim et al. 2022; Nakamura et al. 2022; Sama et al. 2022)

Molecular methods have shown that there is substantial clonal diversity and clonal evolution across metastatic sites of a cancer (Gerlinger et al. 2012). Liquid biopsy provides an overview of all tumor sites contributing to circulating tumor DNA, which can be an important consideration for therapy choice (Badon et al. 2022).

Liquid biopsy also supports two major biomarkers that are required for immuno-oncology, e.g. therapy with checkpoint inhibitors. **MSI** (verifying the presence of mismatch repair deficiency) and **TMB** are both validated in FDA labeling, guidelines, and clinical usage, where both of these can be measured in the newer plasma CGP panels.

Here's where older coding conventions lag PLA conventions. Mismatch repair analysis and TMB are showing up in assay-specific PLA codes, but are absent from the Category I genomic sequencing procedures nomenclature available to all hospitals and labs, even with the January 2023 revisions. For MSI, the College of American Pathologist and the Association for Molecular Pathology have recently produced a major guideline on uniform standards (CAP 2022). However, lacking clear coding and adequate reimbursement, services for MSI and TMB have been underused (Hopkins 2022; Staff 2022). See the recent detailed article in CAP TODAY laying out the adoption and reimbursement issues for tumor mutational burden (Titus 2022).

Given these advantages for plasma-based CGP, acceptance and clinical utilization have been growing rapidly. Already, FDA has approved two distinct tests for plasma-based CGP (one from Foundation Medicine, one from Guardant Health) and there are a range of well-validated lab-developed alternatives. But the policies for coding and payment in genomics tend to lag clinical practice (Trosman et al. 2020; Wong et al. 2022). In the next sections, we will look at coding and then reimbursement for plasma-based CGP.

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The Coding System: Lagging in Specificity

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As recently as 2012, there were only a small handful of AMA CPT codes related to genomics. In 2013/2014, the AMA introduced several hundred codes for genomics across several categories. Generally, single-gene procedures are in the code series **811nn**, **812nn**, **813nn**. Gene panel tests and exome/genome tests are in the **814nn** series, and proprietary molecular tests are in the **815nn** series. In addition to these traditional or Category I code series for lab medicine, AMA has also created almost 400 **"Proprietary Laboratory Analysis"** or **PLA** codes following a different format, **nnnnU**. These codes currently run from 0001U to 0354U, and 20 or more PLA codes are created each quarter. Unlike conventional CPT codes, which require a year or two to produce, PLA codes arise through expedited processes so that just 6 months from the date of application, the code is active and ready for use by labs and payers.

For tumor genomics, there are just a handful of codes for somatic mutation panels. Below, we show the genomic sequencing procedure (GSP) codes, 81445, 81450, and 81455 –with 81455 most closely corresponding with CGP. For the last several years, these codes (shown below) have been defined for DNA-based tests, or DNA and RNA-based tests. Beginning in January 2023, there is a sister code for each of these three codes, reflecting an "RNA only" analysis. The brand-new RNA codes are 81448, 81451, 81456:

Code	Description
81445	Targeted genomic sequence analysis panel, **solid organ neoplasm**, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA,PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed; DNA analysis or combined DNA and RNA analysis
81448	Same; RNA only
81450	Targeted genomic sequence analysis panel, **hematolymphoid neoplasm** or disorder, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA and RNA analysis
81451	Same; RNA only
81455	Targeted genomic sequence analysis panel, **solid organ or hematolymphoid** neoplasm or disorder, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA and RNA analysis
81456	Same; RNA only

In short, the entire laboratory medicine code series, with some 1,500 codes, and hundreds of molecular codes, has had **only 3 codes** specific multi-gene tumor analysis, and those have not been specific to sample source such as plasma or paraffin. While there are **now 6** (by adding the 3 RNA-only) codes, more needs to be done.

While the Category I (80,000-series) laboratory code set has remained static, there has been a proliferation of tumor-specific codes in the PLA code series. Some of the earliest PLA codes were for cutting-edge advances in cancer genomics, such as code **0019U**, for tumor full transcriptome analysis with predictive analytics, and code **0036U**, for combined tumor and germline exome analysis (that is, the patient's germline exome is a comparator for the patient's cancer). CGP codes have ranged from **0048**, the Memorial Sloan Kettering "IMPACT" test, to **0211U**, a Karius test that includes CGP for several hundred oncogenes as well as whole exome sequencing. PLA codes have also reflected new genetic modalities, such as low-pass cytogenomics and optical genome mapping.

Both of the two FDA-approved liquid biopsy tumor gene panel tests have PLA codes, being the Guardant360 CDx test (plasma biopsy, 74 genes, **0242U**) and the Foundation Medicine's FoundationOne Liquid CDx test (plasma biopsy, 311 genes, **0239U**). These tests are described as "CGP," meaning they report across multiple sequence variant types, including SNVs, indels, gene copy number amplifications, gene rearrangements and genomic signatures MSI and TMB.

From PLA to Category I. These examples demonstrate that there is precedence for new technologies and new levels of specificity to appear in the PLA code system prior to the 80,000 series Category I code system. There are also examples where a new technology introduced in the PLA code set and then "graduates" to the Category I code set. As a good case study, once several codes for low-pass cytogenomics appeared under the PLA paradigm, AMA CPT created a universal Category I code for the same service (code 81349). Similarly, the emergence of more PLA codes for liquid biopsy CGP (3 existing PLA codes) and tissue CGP (5 existing PLA codes), may indicate that creation of a code or codes for liquid biopsy testing in the Category I code set is appropriate.

In addition to the increase in FDA-approved plasma CGP tests and LDT-based plasma CGP tests, another justification for creation of a more specific code arises from the consideration of work and resources required. Policymakers aim to consider clinical labor, laboratory work, and other factors that support accurate pricing. Let's turn to this topic in the next section.

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Reimbursement: Appropriate Reimbursement Payment is Possible

Reimbursement: Appropriate Reimbursement Payment is Possible

Under current policies, plasma-based CGP testing impacts appropriate reimbursement, but only for codes that specify plasma-based testing as the underlying technology.

For example, in the Fall 2022 Clinical Laboratory Fee Schedule (CLFS), the FoundationOne Liquid CDx test was priced at $3,500 (code **0239U**), while the Guardant 360 CDx test was priced at $5,000 (code **0242U**). Under conventional coding, where specimen type is not specified but developed for FFPE based CGP testing, code **81455** might have been used, for which CMS reimburses $2919. In other words, when compared to the liquid biopsy CGP CPT codes, the **81455** code designed for FFPE block tests represents an **underpayment of 17-40%,** versus actual reimbursement for these circulating DNA based tests with specific coding.

Plasma-based testing is more resource-intensive in the laboratory. While FFPE based testing can be adequately developed using NGS in the range of 100X depth of sequencing (Robbe et al. 2018), plasma- based testing to identify the "needle in a haystack" circulating tumor DNA – which is often less than 1% of the cell free DNA present in plasma - may require up to 10,000X depth of sequencing or higher (Deveson et al. 2021).

5.1 Kramer et al. 2022: Economics of Plasma Biopsy

In a recent study, Kramer et al. published a cost analysis for molecular testing that showed that this raises the basic lab costs of liquid biopsy testing (Kramer et al. 2023). This is one of the most thorough and careful studies published in the field of genomic micro-costing. Kramer et al. assessed detailed resource and cost inputs for a range of test methods, including conventional PCR, digital droplet PCR, and next generation sequencing. (These approaches are not interchangeable and have distinct purposes, so costs should not be the only method of comparison.)

Of the several methods studied, only next generation sequencing is appropriate to implement CGP. NGS costs are quite sensitive to scale. At lower scale, costs for plasma-based CGP ran as high as $8399-9124, but at larger scale, costs were in the range of current PLA code reimbursement rates ($3500-5000). Like many academic studies, the costs may underestimate real-world overhead costs, and there were no allowances for test development costs and regulatory costs, such as FDA approval. Operating at maximum scale may not always be possible, due to the importance of as rapid-as-possible turnaround times for optimal therapy section.

Based on unpublished data shared through a personal communications by Illumina, a plasma-based CGP assay would cost laboratories over 50% more based on sequencing increase (due to the high depth of sequencing required in plasma). Capital equipment costs increase slightly as well—to account for the platform transition from NextSeq to NovaSeq—however, this represents less than 5% of the total assay cost. Based on these findings, reimbursement rates in the range of the ADLT-based rates noted above (~$4500) adequately reflect the cost of performing plasma-based CGP.

It is important to note that the resources and costs laboratory testing are not the only factors for health systems and payors to consider. A plasma-based approach to testing entirely avoids surgical and image- guided biopsy procedures. Costs for bronchoscopy and biopsy ranging upwards from $3000 (Tailor et al. 2022), even before the costs of FFPE CGP (typically $3000), and the substantial costs of biopsy complications which have now been accurately reported (Vachani et al. 2022). Surgical biopsy costs as well as the real-world complications costs help make plasma-based testing an economically efficient choice in addition to its clinical merits. Recall, as noted above, that plasma-based CGP may be the only and most important way to get biomarker information for clinical decisions.

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Summary

Summary

Over the past ten years, genomic codes on the CMS CLFS have risen from just a few to over 600. New code categories, like PLA codes, have been created and provide an escape valve for rapid coding innovation as new technologies have become available and accepted. **However, it is equally important to keep the Category I CPT codes for genomics up-to-date and available to all laboratories.**

Recently, the AMA CPT adopted revisions in the way tumor genomic codes are handled for DNA versus RNA analyses. This was a very important step, but more needs to be done. For example, areas like microsatellite instability and tumor mutational burden are still entirely missing from the 2023 codebook for comprehensive genomic sequencing procedures.

Similarly, and perhaps even more importantly, the US coding system (CPT) hasn't yet recognized the coding for plasma-based CGP testing, an important area now seeing FDA-approved tests from multiple suppliers and rapid innovation from laboratory-developed tests as well. Payors may have special policies for when plasma-based tests are covered, for what cancers, and under what conditions. Resources for plasma-based CGP tests are different and higher, than for FFPE based tests. Far higher sequencing depth is necessary, and DNA fragment lengths may be shorter, requiring additional bioinformatics development. However, there are also cost offsets obtained by using a plasma-based approach (e.g., fewer biopsies and biopsy-related adverse events).

As of the writing of this white paper in early 2023, there is still a CPT code submission cycle (beginning in **February 2023**) which produces new codes effective as early as **January 2024**. We have time now and through the **May 2023** AMA CPT meeting, to debate these topics and develop the best consensus strategies.

7

References

References

Badon, E. S., et al. (2022). "Clonal diversity in KRAS mutant colorectal adenocarcinoma under treatment: Monitoring of cfDNA using reverse hybridization and DNA sequencing platforms." Mol Cell Probes: 101891.

Benavides, M., et al. (2022). "Clinical utility of comprehensive circulating tumor DNA genotyping compared with standard of care tissue testing in patients with newly diagnosed metastatic colorectal cancer." ESMO Open 7(3): 100481.

CAP (2022). Mismatch repair and microsatellite instability testing for checkpoint inhibitor therapy. CAP_Website.

CMS. (2021). "Next generation sequencing in cancer, NCD 90.2. (2017 for CGP; 2021 for hereditary cancers).".

Deveson, I. W., et al. (2021). "Evaluating the analytical validity of circulating tumor DNA sequencing assays for precision oncology." Nat Biotechnol 39(9): 1115-1128.

Dietz, S., et al. (2019). "Serial liquid biopsies for detection of treatment failure and profiling of resistance mechanisms in KLC1-ALK-rearranged lung cancer." Cold Spring Harb Mol Case Stud 5(6).

FDA. (2011). "Roche Cobas BRAF Test.", from https://www.accessdata.fda.gov/cdrh_docs/pdf11/P110020b.pdf. FDA. (2017). "Foundation One, PMA P170019. ." from https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170019S017B.pdf.

FDA. (2023a). "List of Companion Diagnostics." from https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools#CDx_Table.

FDA. (2023b). "Qiagen Therascreen KRAS Test. ." from https://www.accessdata.fda.gov/cdrh_docs/pdf11/P110030A.pdf.

Foundation_Medicine (2015). Palmetto GBA Publishes Final Local Coverage Determination for Comprehensive Genomic Profiling of Patients Diagnosed with Non-small Cell Lung Cancer (NSCLC) (Press release).

Gerlinger, M., et al. (2012). "Intratumor heterogeneity and branched evolution revealed by multiregion sequencing." N Engl J Med 366(10): 883-892.

Hopkins, C. (2022). "CAP weighs in on MMR MSI assays for immunotherapy patient section. August 8, 2022." Genomeweb.

Imai, M., et al. (2022). "Expert panel consensus recommendations on the use of circulating tumor DNA assays for patients with advanced solid tumors." Cancer Sci 113(11): 3646-3656.

Kim, S., et al. (2022). "Dynamic changes in longitudinal circulating tumour DNA profile during metastatic colorectal cancer treatment." Br J Cancer 127(5): 898-907.

Kramer, A., et al. (2023). "A Micro-Costing Framework for Circulating Tumor DNA Testing in Dutch Clinical Practice." J Mol Diagn 25(1): 36-45.

Nakamura, Y., et al. (2022). "Comprehensive Genomic Profiling of Circulating Tumor DNA in Patients with Previously Treated Metastatic Colorectal Cancer: Analysis of a Real-World Healthcare Claims Database." Curr Oncol 29(5): 3433-3448.

NGS_MAC (2022). Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms (eff. 4/2022).

Olsen, S., et al. (2022). "Real-World Clinical Outcomes after Genomic Profiling of Circulating Tumor DNA in Patients with Previously Treated Advanced Non-Small Cell Lung Cancer." Curr Oncol 29(7): 4811-4826. PalmettoGBA_MAC. (2022). "MolDX: Next generation sequencing for solid tumors. (Eff. 6/2021).", from https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=38045&ver=14.

Pascual, J., et al. (2022). "ESMO recommendations on the use of circulating tumour DNA assays for patients with cancer: a report from the ESMO Precision Medicine Working Group." Ann Oncol 33(8): 750-768.

Quinn, B. (2022). "Cancer patients and access to molecular diagnostics: Understanding the transition toward comprehensive genomic profiling and tumor mutation burden testing. April 2022.", from http://www.discoveriesinhealthpolicy.com/2022/04/reissuing-2022-white-paper-on-tumors.html.

Robbe, P., et al. (2018). "Clinical whole-genome sequencing from routine formalin-fixed, paraffin- embedded specimens: pilot study for the 100,000 Genomes Project." Genet Med 20(10): 1196-1205. Sadik, H., et al. (2022). "Impact of Clinical Practice Gaps on the Implementation of Personalized Medicine in Advanced Non-Small-Cell Lung Cancer." JCO Precis Oncol 6: e2200246.

Sama, S., et al. (2022). "The Role of Serial Liquid Biopsy in the Management of Metastatic Non-Small Cell Lung Cancer (NSCLC)." Clin Pract 12(3): 419-424.

Staff (2022). "Germline genetic testing (MSI) underused in colorectal cancer patients. October 25, 2022." Genomeweb

Tailor, T. D., et al. (2022). "Total and Out-of-Pocket Costs of Procedures After Lung Cancer Screening in a National Commercially Insured Population: Estimating an Episode of Care." J Am Coll Radiol 19(1 Pt A): 35-46.

Titus, K. (2022). "Highs, lows of TMB testing. September 2022." CAP Today.

Trosman, J. R., et al. (2020). "Insights From a Temporal Assessment of Increases in US Private Payer Coverage of Tumor Sequencing From 2015 to 2019." Value Health 23(5): 551-558.

Vachani, A., et al. (2022). "Complications After Transthoracic Needle Biopsy of Pulmonary Nodules: A Population-Level Retrospective Cohort Analysis." J Am Coll Radiol 19(10): 1121-1129.

Vega, D. M., et al. (2021). "Aligning tumor mutational burden (TMB) quantification across diagnostic platforms: phase II of the Friends of Cancer Research TMB Harmonization Project." Ann Oncol 32(12): 1626-1636.

Wong, W. B., et al. (2022). "Alignment of health plan coverage policies for somatic multigene panel testing with clinical guidelines in select solid tumors." Per Med 19(3): 171-180.

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