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An institutional approach to

medical second opinions

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Executive summary

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It's not unusual for medicine to be in the news. But recently, and for good reason, there has been a lot of press about second opinions. Second medical opinions and second surgical opinions are not a new concept. For decades patients have had opportunities to seek a second opinion, but the process and focus has changed over the years. Now, the impact of a second opinion can literally be life-changing and life-saving …as long as the best clinical approach is leveraged. We have found ourselves at the center of a perfect storm – where technology, patient awareness and access to information have collided with an ever-increasing complexity of medical systems, treatments, and protocols. Physicians and patients alike, are being asked to shoulder more responsibility for care, often without access to the best clinical information and resources to make the most informed decision. It is in this storm that the right second opinion program can provide shelter and a safe path forward.

An Institutional Approach to Medical Second Opinions

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Introduction

The practice of obtaining additional medical opinions has been part of the fabric of medical practice since physicians started caring for their patients. The importance of second opinions and peer reviews is now accepted as mainstream and is endorsed by governing medical bodies and opinion leaders worldwide.[1,2,3,4,5]

The complexity of medical diagnosis and treatment has been accelerating exponentially. Recent advances in genetics and molecular medicine (hallmarks of personalized medicine), big data, imaging and other medical technologies, as well as an explosion in research trials, are bringing powerful new possibilities to human health.[6,7]

At the same time these advances introduce challenges to clinicians who are charged with managing all of this complex information. In this context, practitioners working alone may be at a disadvantage to execute second opinions successfully. No individual can be aware of all options. An institutional approach has advantages whereby the multi-disciplinary capabilities of large academic medical centres can be leveraged to support physicians.

Cancer and molecular medicine: an example of growing complexity in medicine

Cancer medicine exemplifies the growing complexity of medical opinions and is the discipline where second opinions are most often requested.[8] Exponential increases in the speed, accuracy and affordability of gene sequencing are ushering in a new era of understanding for both the genetic makeup of the individual patient and the tumor itself. Such understanding allows for highly targeted therapy (sometimes called "precision medicine") whereby cancer tumor characteristics and a patient's genetic profile drive diagnostics, treatment guidelines, clinical trials and cancer knowledge.

Several well known examples have entered the mainstream of cancer care. Tumor marker mutations in the genes p53 (which predisposes to breast and other cancers as well as Li-Fraumeni Syndrome) and BRCA1 and BRCA2 (which predispose to breast, ovarian and other cancers) are helpful to clinicians in terms of prognosis and treatment.[9] HER2 (human epidermal growth factor receptor 2) is an oncogene found on receptor cells of about 30% of breast tumors. The presence of this biomarker is helpful in terms of prognosis and is used to direct therapy towards the monoclonal antibody trastuzumab (marketed as Herceptin).[10,11] New biologic targeted therapies such as Vemurafenib (Zelboraf) targets melanoma[12] and Imatinib mesylate targets fusion mutated protein cells in leukemic cells.[13]

While these genetic markers and associated treatment protocols are now considered standard, new markers are being discovered rapidly. Research in targeted and immunotherapy is quickly adding additional layers of choice on top of these established treatment guidelines. Furthermore, the appropriate sequence of treatment is often unknown and health care providers need to integrate a wealth of information to ensure one treatment does not compromise another. This will continue to usher in complexity for clinicians who must choose optimal care for their patients. Large research oriented medical centres will continue to be a destination for late breaking treatments.

The National Cancer Institute has a list of 12,000 clinical trials currently accepting patients.

In the last several months for example, HER2 therapy in breast cancer is undergoing changes based on results from the CLEOPATRA, TRYPHAENA, NEOSPHERE trials which foist additional nuanced variables on oncologists in the clinical setting. The experimental selective inhibitor drug palbociclib was recently FDA approved for advanced HR positive/Her2 negative cancer after the PALOMA-1 trial announced just last year at the American Association for Cancer Research a doubling of progression-free survival. Such treatment, available at some leading centres, has yet to make its way to mainstream community oncology practice.

In colon cancer, evidence collected from numerous clinical trials is now suggesting that extending RAS (a biomarker) testing beyond the usual KRAS exon (part of a gene) helps clinicians select whether patients should receive cetuximab in metastatic colorectal cancer.[14] Such genetic testing capability for RAS is only available selectively. In lung cancer recently, ALK rearrangements and EGFR mutations can assist clinicians in deciding whether erlotinib and crizotinib are of benefit.[15] Again the molecular

testing is not universally available and its coverage by health plans is variable. And finally in lymphoma, all the treatment options for CNS lymphoma are often suboptimal. This naturally points to the question of whether a patient should enroll in a trial immediately (if available to a patient) or try possibly inferior established methods.

Research trials: an explosion of knowledge

>50 hereditary cancer syndromes associated with genetic markers have been described.

50 approximate genetic markers are associated with breast cancer.

25 with prostate cancer.

10 with ovarian cancer.

Scientists estimate ultimately we will find more than one thousand genetic markers associated with breast cancer and over two thousand with prostate cancer. The National Cancer Institute has a list of 12,000 clinical trials currently accepting patients and over 25,000 that are no longer accepting patients.[16,17]

The sheer size and scope of this landscape is often overwhelming. Solo practitioners will have difficulty being aware of all potential trials and may face obstacles in enrolling their patients in selected studies. Clinical trials are often only available at larger institutions. Such research hospitals typically have dedicated cancer professionals who are tasked with assisting physicians to navigate this maze. Some companies and non-profit organizations offer financial assistance to help patients access medications.[18]

Second opinions help patients and physicians navigate healthcare choices. They are helpful when deciding what targeted agents to give, whether the old regimens or newer ones are "better" for a specific patient, and they can help sort out the relative costs in terms of finances and toxicity. It is worth pointing out that some medications, even though they are approved, may have only a marginal benefit (regorafenib in colorectal cancer and ramucirumab in lung cancer).[19,20,21] Second opinions from those with experience with these new agents can provide important practice changing information for individuals.

Beyond cancer and molecular medicine, each patient needs to have an in-depth discussion with their physician and institutional providers to ascertain whether they are eligible and whether a trial or experimental medicine is a better choice as a treatment option. Non-medical factors can be highly central to this decision making as well and range from considering out of pocket costs for the newest medications to personal tolerance for unknown risks associated with novel treatments.

Delivering second opinions: the importance of communication and process

Even though physicians will understand complex medical information and jargon, the opinion is directly shared with and ultimately utilized by the patient. Institutional approaches can aid in effective communication of the second opinion so that complex information is understood and acted upon effectively. For example, a crucial consideration is to ensure the patient's questions (which may be very different from the referring physician) are heard and answered clearly. Nursing and other health professionals can be embedded into this process to add value beyond what a physician may be able to do.

Part of effective communication also involves appropriate use of information technology. Institutionally-based IT professionals who have access to state of the art systems (such as teleradiology and telepathology platforms) can help to ensure speed, efficacy and user satisfaction when rendering opinions. Having technical and managerial relationships within and across institutions can play an important role in efficiently moving data across firewalls and avoiding bureaucratic impediments.

Not all second opinions are going to require the same amount of time and input. An institutional approach can help ensure that an important guiding principle is adhered to: that consultants should be empowered to go as far as necessary to reach the very best medical opinion. (In the same way we would for an actual patient who is physically present in our hospitals). In the event where a second opinion differs significantly from an original consultation, it may mean having a third or fourth opinion is necessary to clarify a diagnosis and find optimal treatment. This can often mean a further reading of imaging studies or pathology specimens or, where appropriate, engaging consultants from different institutions and centers of excellence.

In complex cases such as rare surgeries or cancer treatments where there may be conflicting information in the scientific literature, and where nuances and subtleties demand the art of medicine be exercised, often the best approach may mean involving several sub-specialists simultaneously discussing a case to reach a consensus (for example, a panel of four oncologists reviewing treatment options on a conference call). Only large institutions will have a critical mass for such real time review. Similarly, where care demands expertise from the full compliment of subspecialties, a multi-disciplinary approach (for example, involving subspecialists in the fields of cytopathology, interventional radiology, radiation oncology, medical oncology, translational scientists and cancer surgery) may be optimal.

Concluding summary

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Patient-focused and highly-specialized care is the best medicine. Providing a second opinion that is based on the same clinical model that is used in the world's leading medical centers of excellence can literally mean the difference between life and death. Having access to a team of specialists and sub-specialists at these centers to determine not only the diagnosis, but also the best clinical treatment plan, ensures the best outcomes for every patient, regardless of where they live. Whether you live in the United States, Canada or other regions in the world, we are all the same species. While medical systems and payment structures may be different – some better, some worse - diseases are the same around the world. Cancer is cancer. The fear of hearing those words, the need for care and compassion and the desire to receive the optimal clinical treatment available is universal. Now, access to the best medical minds from the best medical institutions in the world is available regardless of where you live. Whether you are in Kansas, Toronto, San Paolo, Beijing, Reading or Boston, technology has given us the means to shrink the globe and access the best medicine has to offer.

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In her role, King is responsible for the sales vision, strategy and execution of top-line growth and profit for the North American market. King has over 25 years of progressive experience in the health care industry, starting her career in clinical operations and quality assurance before moving into client facing roles.

Having worked at industry-leading companies like Intracorp, Cigna and most recently, Optum, part of UnitedHealth Group, King is an accomplished leader in organizational design and leadership, sales leadership, client management, process re-engineering and team building.

She received a Bachelor of Arts from Texas A&M University and completed post-graduate work in finance, management and business law.

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Richard Heinzl is a physician, humanitarian and entrepreneur whose current focus is technology and health care worldwide. He is Global Medical Director for WorldCare International, Inc. In this role, Dr. Heinzl provides consultation and oversight on the creation and delivery of medical second opinions to our members worldwide; engages with clients across North America and contributes to the strategic direction of the company.

Earlier in his career Heinzl was the founder of Médecins Sans Frontières/Doctors Without Borders Canada (MSF Canada), which won the Nobel Peace Prize in 1999. He has been a consultant to numerous health ventures, founder and CEO of MediSpecialist.com Corp., a dot-com era second opinion company and CEO of CardioView Inc., a medical imaging company in the field of cardiology.

He is a graduate of McMaster University's DeGroote School of Medicine and completed postgraduate degrees related to global health at Harvard University and the University of Oxford. He is a Fellow of the American College of Preventive Medicine. In 2000 he received an Honorary Doctorate (LLD) from McMaster University and was named one of the "Hundred People Who Make a Difference" in Canada by Penguin Books. His Memoir, "Cambodia Calling" is published by Harper Collins.

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