

## **Silver linings — an opportunity to improve clinical paradigms following the COVID-19 pandemic**

The COVID-19 pandemic has greatly disrupted clinical workflows and standard management algorithms. Many hospitals have responded to infection risks and resource constraints accordingly by curbing non-urgent procedures and demarcating the number of ICU beds that patients without COVID-19 can occupy;<sup>1,2</sup> as a result, clinicians have been tasked with devising alternative management approaches that comply with these limitations.

One field that has drastically changed its practice during this period is clinical oncology. Not only are cancer patients particularly vulnerable to COVID-19 given their immunocompromised state, but certain cornerstones of treatment paradigms — particularly invasive surgeries — can drain limited resources and potentially result in complications that necessitate ICU-level care. Optimal treatment plans during the pandemic are thus often ones that stabilize malignancies while minimizing infection risks and resources consumed.

Although this shift imposes an immense burden on care providers and cancer patients, it also presents an unprecedented opportunity to reconsider, refine, and revise long-standing paradigms in clinical oncology — even after the pandemic subsides.

This realization was exemplified by a team of oncologists at Massachusetts General Hospital (MGH). The physicians had been treating a 58-year-old man with a melanoma of the left cheek that metastasized to the neck, lungs and adrenal glands. Having exhausted numerous treatment options, the patient was initiated on immunotherapy and fortunately experienced a marked early response; however, he soon developed acute rejection of a renal allograft transplanted over fifteen years prior. From an oncologic standpoint, the priority was to dampen the local inflammatory response while eschewing systemic immunosuppression and minimizing any break from the efficacious immunotherapy. Additional pandemic considerations included reducing the patient's infection risk by shortening his time in the hospital and conserving scarce resources such as a ventilator and ICU bed. While embolization or surgery normally would have been the top considerations, the risk and cost of potential complications was felt to be too great under current circumstances. The multidisciplinary team conducted a deep literature dive to rediscover dusty articles published twenty years ago that suggested the use of low-dose external beam radiotherapy (EBRT) for managing acute renal allograft rejection.<sup>3</sup> Ultimately, radiotherapy was felt to be the best option for achieving a balance of the above goals but likely would not have been considered before the pandemic.

This patient provides just one of many cases that will facilitate a closer look at alternative treatment options that normally would not be given much thought but are suddenly thrust into the limelight out of necessity. For instance, extended neoadjuvant therapy is now frequently advised in cases for which upfront surgery would have been pursued in the past;<sup>4</sup> in fact, institutions including MGH have established virtual tumor boards to remotely triage such patients, bringing together medical oncologists, radiation oncologists, surgeons, radiologists, and other providers in a collaborative manner.<sup>2</sup> In the United Kingdom, hepatobiliary cancer operations have been entirely deferred, so the BILCAP study group reached out to their counterparts at MGH to collaborate on consensus guidelines for definitive radiotherapy of biliary tract cancer during the pandemic. Since then, Germany, France, and Australia have joined in to adopt the same guidelines. In addition to aiding infection control and resource allocation, this initiative could provide insights that impact how patients with inoperable biliary tract malignancies are managed in the future — an opportunity that may have never arisen if not for the circumstances of the COVID-19 crisis.

Over the past two decades, the technology underlying the planning and delivery of radiotherapy has improved dramatically and, coupled with our improved understanding of normal tissue response to radiation damage, has enabled hypofractionation by safely delivering larger doses over a shorter treatment duration. In some cancer types such as breast and prostate carcinomas, significant evidence has accumulated in support of the efficacy and safety of such hypofractionated regimens, although there has been relatively slow adoption in the United States.<sup>5,6</sup> However, constraints imposed by the COVID-19 pandemic have forced temporary acceptance of hypofractionation, even in cancer types where little guiding evidence exists. Tracking outcomes in these instances will be critical: if hypofractionation achieves similar oncologic results while minimizing healthcare exposure, treatment costs, patient inconvenience, and clinical crowding, adopting this technique could benefit many parties even after the pandemic passes, particularly in radiotherapy resource-limited regions. Furthermore, particle therapy such as proton therapy is characterized by dosimetric advantages that can significantly decrease normal tissue toxicity compared to conventional photon treatment. In the setting of preoperative chemoradiation for esophageal cancer, the decreased toxicity associated with proton therapy manifests as reduced surgical complications and need for ICU admissions.<sup>7</sup> Radiation oncologists in the Netherlands have been using this approach during the COVID-19 pandemic, and current circumstances may accelerate the widespread adoption of preoperative particle therapy where available.

The pandemic has afforded clinical oncology and other fields a unique opportunity to ascertain whether conventional practices are indeed as optimal as once believed. If we establish appropriate clinical trials

and thoughtful cohort studies based on our collective observations during the COVID-19 pandemic, we could very well learn more convenient, efficient, and resourceful ways to obtain better outcomes for patients. Indeed, a handful of initiatives such as the PanSurg PREDICT Project have been established to accomplish these very goals.<sup>8</sup>

Patient physical health is not the only outcome to monitor following these unprecedented disruptions in routine protocols; some clinical workflow changes could also serve patient satisfaction, physicians, hospitals, and even the environment. For instance, many consultations routinely conducted in person have been moved to virtual platforms as a result of the pandemic,<sup>1</sup> allowing patients, family members, and caregivers to speak from the comforts of their homes and other convenient locations, decreasing the frequency of hospital visits, and reducing travel and opportunity costs for those involved. This reduction in travel could also considerably benefit the environment. Harvard University recently told faculty members that its greatest barrier to being carbon neutral is their academic travel — that no matter how energy-efficient a car someone drives, it cannot offset a single international plane ride. Imagine if some providers did not drive to their offices daily and patients did not fly great distances for consultations — if thousands of physicians did not travel to attend medical conferences — because these meetings were held virtually. The carbon footprint of the medical field would be remarkably lighter, and the pandemic has taught us that this prospect might not be as impractical as it once might have seemed.

It is undeniable that COVID-19 has placed the clinical world under immense stress, that it has devastated patients, families, care providers, and hospitals in many ways. Keeping these truisms at the forefront of our minds, we urge the community to search for potential lessons that will serve us well, perhaps allowing us to provide even more responsible and optimized care after the pandemic. Even in the most dire of circumstances, we can create silver linings if we are prepared to recognize them.

## References

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