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Short Communication

Novel Life-Saving Radiotherapy Technology and How it Can be Made Available in the Developing World

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The COVID-19 pandemic has highlighted how globally interconnected health of individuals has become, and how international co-operation is needed to combat disease. This is not just with communicable diseases, but with non-communicable disease like cancer too. Due to the lack of in-person interactions at conferences due to the pandemic, there has been an avalanche of webcasts from vendors selling the newest novel health technologies such as the latest radiotherapy equipment, with presentations from oncologists on the wonderful results that they are getting using these technologies in oncology centres predominantly in the US and Europe.

Some examples of the new technologies are FLASH-radiotherapy and the MRI Linear accelerator, in addition to a slew of (claimed to be) machine learning and artificial intelligence radiotherapy planning systems, such as those from RaySearch Laboratories.

FLASH-radiotherapy delivers radiotherapy at a much faster rate than conventional radiotherapy. Traditionally the daily dose of prescribed radiotherapy is delivered by todays linear accelerators in a few minutes, but FLASH-radiotherapy systems, such as the FlashKnife from PMB Alcen, can deliver doses of radiotherapy in a fraction of a second. It has been shown in animal models to improve what radiation oncologists refer to as the therapeutic ratio. An improvement in the therapeutic ratio is when you can increase damage to the cancer while causing less damage to the surrounding normal tissue. It is postulated that cancer cells may be more susceptible to damage by radiation if delivered at an extremely fast rate, while normal tissues seem to be much less affected by radiation delivered at a faster rate. This technology has shown promise in treating cancers in animal models i.e. destroying more tumour cells while causing less damage to the surrounding tissues, and safety was established in the first human patient [1].

The more mature technology is the MRI linear accelerator which combines an MRI scanner and a radiotherapy linear accelerator. Despite the improved visualisation of many tumours with MRI as opposed to CT scanning, combining an MRI scanner and a linear accelerator to visualise the tumour while treating it with radiotherapy has been a challenge in the past due to the distortion of radiation in the MRI magnetic field. One of the pioneers in solving this problem is the MRIdian from Viewray, which has a MRI scanner combined with a linear accelerator, allowing the radiation oncologist to see the tumour via the MRI while it is being treated with radiation. This allows accurate radiotherapy to be delivered to areas which traditionally could not receive high doses of radiotherapy e.g. pancreatic tumours. In the case of pancreatic cancer, the dose of radiotherapy which could traditionally be delivered was constrained by:

1. The sensitivity of the surrounding bowel to radiation, leading to radiation induced side effects if doses required to cure a pancreatic cancer were delivered to even a small part of the stomach or small bowel.
2. The movement of the pancreas (and pancreatic tumour) continually with respiration as the treatment is delivered.

These first 2 constraints can be overcome with traditional CT image guided and respiratory gated stereotactic body radiotherapy techniques. The reason why it was still not possible to get adequate doses of radiotherapy into tumours in organs like the pancreas was due to the fact that tracking of a cancer on traditional body radiosurgery hardware uses a combination of surrogate markers such as watching the patient's chest movements to infer the movement of e.g. the pancreatic tumour and on-board CT scanner imaging of the tumour, which in the case of pancreatic cancer, is very inaccurate.

This led to a lot of uncertainty for the treating radiation oncologist with regard to not overdosing the bowel surrounding the tumour while delivering the radiosurgery, and subsequently resulted in them prescribing doses of radiotherapy which are not adequate to cure a pancreatic cancer, or risk causing morbidity in the patient. This has contributed to the traditionally poor survival rates from pancreatic cancer.

The MRI Linac has enabled the oncologist to now track the tumour in real time visually, without the use of surrogates, and enable her to be confident that the doses of radiation are being delivered to the target (pancreatic tumour), and not to the bowel in very close contact with it. In current on-going clinical trials, it has enabled radiation oncologists deliver a dose of radiotherapy to the tumour which is almost radio-biologically double what has traditionally been prescribed, and although follow-up of treated patients is still short in most of the clinical trials, the preliminary results look excellent-potentially providing a cure to some patients who previously would have succumb to the disease, and further investigation is being recommended [2]. An added benefit which emerged of treating this way during the COVID-19 pandemic, is that due to

the accuracy of the treatment, radiotherapy could safely be given in much larger daily doses, meaning fewer visits to the oncology department and lower potential infection exposure for patients who are already at high risk of getting severely ill from hospital acquired infections.

There is however a high price tag attached to these new technologies. The cost of an MRI linear accelerator is at least 3-fold higher than the cost of a conventional linear accelerator capable of body radiosurgery. However, reimbursement from funders for radiosurgery in the private sector is a fixed rate regardless of the technology used. Radiosurgery is seen to be a commodity rather than a differentiated product, but as we can see from the example of the MRI Linac, it is anything but a commodity. There are clinical settings where specific types if radiosurgical equipment is needed which should be remunerated at different rates depending on the technology used. The bizarreness of the situation could be likened to all chemotherapies being remunerated at the same rate irrespective of the compound used, or the indication for which it is used. Hence, ideally, a modified rate should be charged if these new technologies are used. This may be possible if funders are approached to do this, but first, the technology needs to be available in the country. This would mean that potential investors in this technology would need to procure this equipment, and set-up the oncology centre while also taking on the risk that they may not be remunerated for treating patients with the superior technology if funders decide to maintain the status-quo.

This has led to potential investors in such equipment being reticent to invest in it, especially in countries like South Africa. The unfortunate reality is that potential investors in such technology, such as health-care private equity and venture capital (PEVC) funds in countries like South Africa, are much less risk seeking than counterparts in the United States and Europe. Even though there is large potential financial benefit of bringing in this technology, they are not willing to take on the added risk, rather sticking to the already long-established equipment. There is no real health-care venture capital or private equity in South Africa, as true PEVC funds should be willing to take on high risk for large potential returns, and the way PEVC funds behave in South Africa is more similar to traditional debt financing. The incumbents in radiotherapy treatment in South Africa, which is effectively a duopoly between a national hospital group which offers radiotherapy services, and a private company specialised in radiotherapy equipment centres, have little incentive to invest in the novel radiotherapy technologies as they treat most of the patients on their commoditised equipment already, and hence do not want to risk extra capital expenditure to bring in promising new, unproven but potentially life-saving therapy. It has resulted in old technologies such as the GammaKnife which has been in Europe and the United States since the 1960's finally making it to South African shores recently, and now being marketed as novel technology, when it is clearly not. The risk is that the contribution of South Africa to radiation oncology research will fall away, in addition to patients in South Africa not reaping the benefits of these new technologies. The opportunity is that it does leave the market in specialised radiation oncology open for a group focusing on niche highly specialised radiotherapy treatments.

The solution lies in disrupting the current model of radiotherapy being found in or near general hospitals, in favour of creating stand-alone centres which have only novel radiotherapy technologies. The centre would not be affiliated to any hospital but would be a value adding centre for patients diagnosed with specific cancers in a general hospital to be referred to for their therapy. Due to the specialised equipment which this requires, it would be remunerated at a higher rate. Also, due to the fact that most one stop shop general hospitals and general oncology centres would not have this equipment, as they usually purchase equipment which could generically treat most cancers, such a specialised unit would get referrals from the general hospitals and general radiotherapy units, while general units would retain most of their current patients. This would allow the new technology to be used more as it would drain patients from many centres, making the initial capital expenditure in its purchase more attractive.

Another option, other than a true PEVC fund purchasing the new technology and setting up these centres, is for vendors of this high-cost specialised radiotherapy equipment to stop viewing themselves as manufacturers of equipment selling to oncology service providers, and to rather move from the manufacturing industry to the service industry. They could, and should, vertically integrate by developing oncology centres themselves, and offering radiotherapy service centres for radiation oncologists to book their patients. This would allow them to earn an ongoing stream of income from the machines they manufacture, while also making their technology more widely available. By having more patients treated on their equipment, clinical trials validating the benefits of the technology could be available quicker, as recruiting of patients would be much faster. Further, it could serve to reduce the ability of competitors with similar equipment from selling it in a particular market, as the need for such centres would often be very limited, and once one highly specialised centre exists, there would be very little need for a second in the same market.

Although such a business case seems intuitive, it has not happened yet because it requires a restructuring of several aspects of the health ecosystem. First, remuneration can no longer occur on a fee for service basis but will need to occur as a fee for diagnosis. It has already been shown in Michael Porters HBR review article from 2013 [3] that payment for diagnosis creates value for funders, providers, and patients. Secondly, hospital groups can no longer view themselves as one stop shops, conflating the business models required for patients coming in looking for a solution for their problem (where fee for service works well) and that of actually delivering a specialised therapy, where increasingly, a fee for diagnosis works well. Once technologies in treatment become mature, and combined with other healthcare innovations, like artificial in-

telligence driven big data analysis, and the genomics of cancers, we would then be entering the realm of precision medicine, where highly specialised cancer centres managing only certain cancers could charge a fee for outcome, rather than a fee for diagnosis.

The other side of oncology in South Africa is in the public sector, where the focus has mainly been on reducing the long waiting lists of patients requiring radiotherapy. There has traditionally been a tendency in the state facilities to do the radiotherapy in-house despite their lack of facilities, rather than partnering with private oncology centres to have state patients treated in private facilities which often have excess capacity. However, the creation of the standalone novel radiotherapy centre provides a unique opportunity for the state to have state patients treated at these facilities, and they could look at various business structures to make this happen. For an up-front investment, the state will contribute to the purchase of the machine (together with a PEVC funder), in exchange for patients from the state sector who fulfil the clinical requirements for therapy on the machine having access to it. The private equity funder would thus be needed to make a smaller investment but still be responsible for the running of the machine. This would have the effect of leveraging their investment in the novel technology, making such an investment much more attractive to them, as they could retain profits while lowering risk and capital expenditure. The state would have the benefit of being able to provide treatment to its patients that they would ordinarily have not had access to.

The overall result is more patients getting access to lifesaving treatment. An added benefit eluded to earlier, is that patients could be recruited for clinical trials quicker, proving the efficacy of such treatment, allowing the novel therapies to be refined and improved much quicker. The clinical trial process should also be restructured, with it no longer being a final test to a hypothesis (e.g. patients treated with 10Gy X 5 fractions to the pancreatic tumour have improved survival) but rather part of an iterative process, where the therapies are refined as investigators start to see the results of treatment. Having patients being more quickly recruited from more centres will fast-track this process. The COVID-19 pandemic has highlighted the need of how an overhaul of the clinical trial process is needed to get lifesaving treatments safely on the market faster, and cancer therapies are no different.

In conclusion, the high price of novel technologies in cost intensive specialities like oncology has been a barrier to access in many developing countries like South Africa. However, with a restructuring of the PEVC funding of such projects, remuneration of therapies, set-up of healthcare facilities and running of clinical trials, access could be expanded. Furthermore, by using these technologies in the developing world, and getting outcome data of their treatments, efficacy data from the use of new technologies could be made available more quickly, and treatments refined faster, allowing for more patients globally to be cured from their cancers with less side-effects.

Bibliography

1. Bourhis J., *et al*. "Treatment of a first patient with FLASH-radiotherapy". *Radiotherapy and Oncology* 131 (2019): 18-22.

2. Rudra S., *et al*. "Using adaptive magnetic resonance image-guided radiation therapy for treatment of inoperable pancreatic cancer". *Cancer Medicine* 8.5 (2019): 2123-2132.

3. Porter Michael E and Lee Thomas H. "The Strategy That Will Fix Health Care". *Harvard Business Review* 91.10 (2013): 50-70.