The Field of Radiogenomics

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Traditionally, cancer patients with similar cancers and tumor stages, regardless of the molecular and radiological characteristics of the tumor, have been treated with the same chemotherapeutic agents. This approach was controversial, as studies demonstrated that protocols which were effective for some patients were not effective for others, despite similarity in patients’ cancer type and stage. This variance in the treatment success led to a new notion in cancer management, the creation of separate and individualized treatment plans for each distinct cancer patient. This personalized approach is being increasingly utilized as it results in improved outcomes through refining the diagnosis, stage, and treatment of the patient. In order to develop a personalized treatment plan, physicians must first learn about the cancer patient’s genetic basis and the molecular structure of their tumor. This learning will enable physicians to develop novel treatment strategies which will be more effective and thus associated with less adverse side effects than that of standard cancer treatments. With the continuous expansion of knowledge in the field of genetics, including a greater understanding of the pathway mutations involved in cancer, researchers found that genetic differences in cancer patients can influence treatment methods and can explain many of the different responses to these treatment protocols. Additionally, these genetic studies demonstrated that some genomic signatures, which are responsible for cancer development, could also be used as treatment targets. These markers led to the advent of targeted therapy, a new treatment approach which commonly results in significantly improved prognoses for patients. This approach of targeting specific tumor driver molecules led to the concept of personalized medicine. Thus, the advanced genetic analysis of cancer through the personalized medicine approach can provide physicians with the tools needed to create individualized treatment plans for each patient.

Studies analyzing the effectiveness of the ’smart’ drugs targeted to the specific mutated genetic pathways of the certain cancer types has gained popularity in recent years. In a study by Ross et al. human epidermal growth factor receptor (HER-2) oncogene, encoding a transmembrane tyrosine kinase receptor, was analyzed as a target for breast cancer treatment [1]. In this highly-detailed review, the articles in the literature about the anti–HER-2 targeted therapies have been discussed and in the conclusion stated that this treatment approach is a significant and efficient breast cancer treatment, especially when combined with cytotoxic agents. For this reason, it was proposed that whenever possible, HER-2–positive breast cancers must be subclassified for the opportunity to benefit from anti-HER smart drug medications like as trastuzumab and lapatinib. Additionally, it was suggested that HER-2–negative patients must not be misclassified as HER-2 positive due to the cost and potential adverse effects of these drugs when these patients have very little chance of receiving clinical benefit from the treatment.

In another study by Lynch et al. Epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer (NSCLC) patients were analyzed in order to determine if they have any response to tyrosine kinase inhibitor gefitinib [2]. This ’smart’ drug has been proven to be very effective for about 10 percent of the patients studied. To understand the molecular mechanism underlying this specific response to gefitinib, Lynch and co-workers had analyzed somatic mutations in the tyrosine kinase domain of the EGFR gene. In conclusion it was stated that a subgroup of patients with NSCLC have specific mutations in the EGFR gene, which correlate with clinical responsiveness to the tyrosine kinase inhibitor gefitinib.

Future studies are in progress to determine other possible mutated genetic pathways and to develop new smart drugs for a personalized cancer treatment. Nevertheless, this genetic-based personalized medicine approach is an expensive, time-consuming and invasive procedure, which requires tissue biopsy and sampling. Another limitation of this approach is that the tissue sampling is most often obtained from a specific location of the lesion and for this reason, does not entirely represent the lesion’s unique anatomic, functional, and physiologic properties, such as size, location, and morphology. Therefore, a non-invasive, widely available, easy-to-apply, reliable and inexpensive method would be of great importance. Radiographical imaging tools are known to meet these needs, which have the potential to assist in the development of personalized cancer treatment and are very useful for diagnosis, staging, and treatment planning.

Several studies in the recent literature have shown that there are some important correlations between radiographical imaging features of different cancer types and specific mutated genetic pathways, which can be considered as a novel method for the detection of radiological imaging traits. This new field was introduced as ’radiogenomics’ [3] and has started to be used in a broad spectrum especially for cancer researches and personalized medicine. Additionally, similar to radiogenomics, analysis of large amounts of advanced quantitative imaging features from standard radiographic evaluations has begun to be used for the quantification of the prognostic associations between images and the medical outcomes of personalized medicine for specific cancer types. In this field, however there is no correlational analysis of genetic basis and the radiological imaging traits, this new approach was named as ’radiomics’. It is claimed that the radiological imaging traits or the radiophenotypes can serve as surrogates of mutated genetic pathways which have mainly two major advantages:

1. To understand the molecular basis of the tumor subtype without the need for invasive procedures;
2. To enable the physicians develop targeted treatment methods for each individual patient.

Hence, the main role of radiogenomics is to simply create imaging
biomarkers that can identify the genomics of a cancer patient and aid to guide the treatment with specific smart drugs for each individual without the need of a biopsy and genetic analysis.

In the last decade, the field of radiogenomics has evolved considerably in parallel with the ongoing studies. Many studies have managed to find associations between the imaging features of some cancer types and molecular properties of that cancer which leads us to choose the correct treatment regimen; therefore affecting the overall survival of the cancer patients. In one of these studies, it was concluded that, imaging trait of tumor contrast enhancement which predicted the activation of hypoxia gene-expression program, can be used as a biomarker for selecting glioblastoma multiforme (GBM) patients for antiangiogenic therapy [4]. In another study, the researchers identified specific Magnetic Resonance Imaging-Fluid attenuated inversion recovery (FLAIR) features as imaging surrogates for cellular invasion and migration for GBM patients which also have potential therapeutic significance since successful molecular inhibition of invasion will improve therapy and patient survival in GBM [5].

Similar successful relations of imaging traits were also defined for liver cancer patients based on CT images. In a study by Segal et al. it was shown that the presence of “internal arteries” on Computerized Tomography images of liver cancers are associated with the occurrence of microscopic venous invasion among the patients with related genes [6]. There are similar studies in the literature including other cancer types such as colorectal cancer, NSCLC, breast cancer etc. and their imaging traits for specific mutations which are predicting factors for cancer types such as colorectal cancer, NSCLC, breast cancer etc. and their imaging traits for specific mutations which are predicting factors for targeted treatment. So, in short, the field of radiogenomics covers all these potential pathways in order to understand the possible mechanisms of cancer development and to tailor a personalized approach for individual cancer patient. It allows us to make an assessment of many different mutated cancer pathways with the help of radiologic imaging traits.

Future Directions

The era of radiogenomics is rapidly expanding for the last couple of years. It is believed generally in the medical sciences that this new approach has the great potential to improve the health care system for the cancer patients by creating links between radiologic imaging traits and specific molecular biomarkers of the cancer. Now, we know that, the use of imaging phenotypes as a surrogate for these specific cancer biomarkers is a quick and reliable method. Nevertheless, there is still much work to do as cancers have a great variety. Future studies are in progress to find out other possible correlations between the imaging features of certain cancer types and attendant molecular structures permitting reliable diagnosis, accurate staging, proper prognosis and optimal therapy.

References