Clinical support tool- Interstitial Fluid Velocity Assessment of Solid Tumors from MRI (Tel Hashomer)
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Clinical support tool- Interstitial Fluid Velocity Assessment of Solid Tumors from MRI

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Background

The consequences of high tumor interstitial fluid pressure. Fluid pressure in the tumor's interstitial space is a major force characterizing solid tumors. At the tumor interface with normal tissue, a steep drop in pressure causes fluid to rapidly leak out of the tumor. This peritumoral interstitial fluid velocity (IFV) drives the outflow of drugs, secreted factors and metastatic cells, thereby, restricting drug delivery and facilitating invasion.

Implications for developing a clinical tool for IFV estimation. Estimating the efficiency of drug delivery can be used as a predictor of resistance to therapy. Predicting the response of tumors to therapy is highly important in the neoadjuvant (pre-operative) therapy setting. Neoadjuvant studies are one of the critical components of the novel adaptive clinical trial design that allows rapid testing of new regimens, exploiting the response to therapy as an end-point. Therefore, it is crucial to consider physical parameters that restrict drug delivery into the tumor. Evaluation of tumor IFV can assist in testing new therapeutics or approaches that reduce affect tumor physiology, thereby increasing drug uptake and the chance of successful treatment. Finally, high fluid pressure has been shown to be associated with metastasis and with clinical outcome, hence, its routine assessment can have an important prognostic value.

Because of its clinical importance, a ***non-invasive*** routine estimate of tumor IFV might have a ***profound effect on the assessment and treatment*** of many solid tumors. The available techniques for fluid pressure measurement are performed by invasive needle insertion and thus are not suitable for routine assessment of tumors. A recent study used a physical model to evaluate peritumoral IFV and showed high correlation to standard pressure measurements, as well as to clinical parameters. However, this study was based on manual analysis, making it difficult to implement as a routine clinical tool.

The Need

High peritumoral interstitial fluid flow velocity (IFV) facilitates outflow of drugs, secreted factors and metastatic tumor cells, and is a recognized driving force for metastasis.

Despite the established role of IFV in resistance to therapy and in invasiveness, the measurement of IFV in the clinical context is limited and poorly understood due to a **lack of an efficient way** to measure it in patients.

Although many efforts were invested in predicting response to treatment, tumor subtype and molecular biomarkers only partially explain the high percentage of non-responders. Therefore, in addition to biomarkers, it is crucial to estimate physical parameters, such as IFV, that restrict drug delivery into the tumor, as they may be critical unexplained factors in tumor resistance to therapy.

The Technology

We have developed a non-invasive and automatic assessment of peritumoral interstitial fluid flow velocity (IFV) derived from routine MRI examinations. The method is based on a recent physical model that assesses IFV. Previous measurements used manual analysis, making it difficult to implement as a routine clinical tool.

Our method implements advanced image processing techniques to automatically track the expansion of the tumor contour over time. Fluid flow velocity is calculated accordingly and mapped throughout the peritumoral regions (Figure 1).

In our preliminary studies we applied this method to measure peritumor flow velocity for breast cancer patients that underwent neoadjuvant treatment. We found a significant difference between tumors of responders and non-responders (Figure 1). The results suggest that this method may assess efficacy to drug delivery and may predictive response to therapy.

Advantages and innovation of the method:

Non-invasive method for assessing peritumoral interstitial fluid velocity and the tumor drug delivery efficiency - no need for painful needle-based measurements.

Automatic algorithm that needs minimal intervention from the radiologist (contouring).

Independent of the MRI protocol, thus allowing for **retrospective** analysis of datasets and implemented to routine MRI studies.

Potential Applications

The Product: Clinical Decision Support tool. Disease management tool for all solid tumor; abnormal mass of tissue that usually does not contain cysts or liquid areas.

Estimating barriers to drug delivery can determine which patients would respond well to pre-surgical therapy, preventing ineffective treatments and improving treatment plans (**predictive** tool).

Understanding the role of fluid flow on tumor invasion and metastasis and identifying targetable elements to prevent metastatic spread. (**Prognostic** evaluation).

Clinical measurement of tumor fluid flow can facilitate **drug development** of agents that increase drug delivery and improve treatment outcome.

Incorporating the tumor biophysical properties into the new generation of clinical trials (**adaptive trials**) that uses patient's tumor profile can accelerate the process of drug approvals.

The Market

Our proposed product is par of the solid tumor prognostic and precdictive market, to follow up needs to achieve better treatment for the patient.

The major driving factors for the growth of this market include increasing incidences of solid tumors, rising prevalence of different forms of metastatic cancers, increasing demand for highly effective chemotherapeutic agents and ripe pipeline of drugs which is available in the global market. According to World Health Organization (WHO), approximately 8.2 million people died due to different types of cancers worldwide in 2012. Among them lung, colorectal, breast and liver cancers were among the leading causes of cancer deaths. Most common forms of solid tumors include brain tumors (medulloblastoma and glioma) and neuroblastoma; other less common solid tumors include rhabdomyosarcoma and osteosarcoma.

Cancer testing is maturing from personalized medicine to precision medicine, where molecular biomarkers and Imaging technologies are essential for precise diagnosis, therapy selection, therapy monitoring and early detection of cancer recurrence.

The global cancer diagnostics market size was valued at USD 124.0 billion in 2016 and is expected to grow at a CAGR of 7.2% over the forecast period. Growing prevalence of oncologic cases, constant technological advancements in diagnostics, and increasing demand for effective screening tests are some of the prime factors spurring the demand for screening tools across the world. In addition, rising awareness and supportive government initiatives are some additional factors that are anticipated to boost the growth of the sector during the forecast period.

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