

Personalized nanodiagnosics of prostate cancer. A proposal for repositioning genetic testing on the timeline of the diagnostic and therapeutic process

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Prostate cancer (PC) was the most commonly diagnosed malignant tumor in men in Poland in 2019 (20.6%) and the third leading cause of cancer-related deaths in men (10.3%), following lung and colorectal cancer. According to the National Cancer Registry, from 1985, when 2,010 new cases of PC were reported, to 2019, when 17,638 new cases were noted, there was a consistent over eightfold increase in PC incidence. Despite advances in both radical and palliative therapies for PC, there has also been a continuous increase in mortality. In 2019, 5,618 deaths from PC were recorded.

Early and comprehensive diagnostics are crucial in determining the treatment approach and the ultimate outcomes for PC. Transrectal prostate biopsy guided by transrectal ultrasound (TRUS) combined with multiparametric magnetic resonance imaging fusion – Bx MRI/US (fusion biopsy) – is an effective method for PC diagnosis (with a detection rate of up to 68.4% in the "fusion part" of the biopsy combined with systematic prostate biopsy). When additional clinical data and parameters from the diagnostic process (such as patient age, pre-cancerous conditions in previous biopsies, digital rectal examination results, total and free PSA levels in blood serum, prostate volume from TRUS, and PSA derivatives such as PSA density (PSAD) and the free-to-total PSA ratio) are considered using the CART classification tree method for determining indications for Bx MRI/US, this diagnostic tool achieves a sensitivity of 94%, specificity of 84%, and diagnostic accuracy of 90%.

Alongside histopathological studies, genetic testing results are becoming a valuable new source of information that allows for the personalization of both the diagnostic and treatment processes. The material most commonly available to geneticists consists of archived paraffin blocks containing tissue used in HP diagnosis. Even the most meticulously conducted HP procedures can affect the quality and quantity of DNA available to geneticists, not to mention the point in the diagnostic and therapeutic process at which this occurs. We present a method for obtaining prostate biopsy specimens that enables the isolation of high-molecular-weight DNA, meeting the qualitative and quantitative criteria necessary for conducting next-generation DNA sequencing (NGS). We obtained 37 biopsy specimens from 13 patients and standardized the isolation process, consistently obtaining high-molecular-weight DNA samples (5.8 µg/ml - 57.2 µg/ml). The samples were obtained from a single biopsy applied to a membrane using the SmartBx device. In four cases, NGS sequencing was performed using DNA samples from six biopsies, achieving very high-quality parameters (mean sequencing depth ~780x). This allowed for the detection of genetic variants even in a small percentage of cells. These studies are preliminary, preceding the formulation of the final objectives for a new research project.

[1] Centrum Onkologii – Instytut im. Marii Skłodowskiej-Curie. Krajowy Rejestr Nowotworów; <https://onkologia.org.pl/>

[2] Wojciechowska U. i inni: Nowotwory złośliwe w Polsce w 2013 roku. Warszawa, Centrum Onkologii – Instytut im. Marii Skłodowskiej-Curie. Krajowy Rejestr Nowotworów; 2014 r.

[3] Wilkosz J. i inni: Zastosowanie metody drzew klasyfikacyjnych CART (Classification and Regression Trees) w ustalaniu wskazań do przezkroczowej biopsji stercza nadzorowanej obrazowaniem z fuzji wieloparametrycznego magnetycznego rezonansu jądrowego z przezodbytniczą ultrasonografią gruczołu krokowego w diagnostyce raka stercza - analiza 86 własnych przypadków 49 Kongres Naukowy PTU, Katowice 12.06.2019