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Modern Interpretation of the Role of Hormone Therapy in Prostate Cancer

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Abstract: According to the World Health Organization (WHO), the incidence of prostate cancer is constantly increasing all over the world, and it is the third most common cancer in our country, after malignant tumors of the lung and stomach. Up to 40% of men between 60 and 70 years of age and 70% of men over 80 years of age have various stages of prostate cancer [1, 4].

Due to the specific characteristics of the clinical course, the prostate tumor may not only not affect the patient's well-being for many years, but also may not manifest itself in any way. The results of modern studies have shown that none of the currently used non-invasive methods can provide one hundred percent information about the presence of prostate cancer [2, 3].

In this regard, in order to improve the diagnosis and detection of oncological process in the prostate gland in the early stages, the revolutionary HistoScan device was created and is being successfully used [5]. It is a patented technology for differentiation, characterization and imaging of prostate tissue based on ultrasound backscatter analysis. This device can perform an ultrasound examination of the prostate gland with a high degree of accuracy, identify areas of suspicious tissue for cancer. Thus, the histoscan makes it possible to suspect prostate cancer (T 1 - T 2 stages). By displaying this information in the form of a 3D model and a map of the prostate, it is possible to determine the location and size of tumor tissue, to obtain targeted tissue samples during biopsy, to reduce the number of tissue columns of biopsy material, as well as to reduce the non-radical condition. allows observation. cancer therapies, and furthermore, we consider the possibility of targeting using histoscan mapping during focal therapy for prostate cancer.

Key points: Materials and methods, Histoscanning map, Prostate sextants.

Materials and methods

Our work was aimed at identifying people with prostate cancer, checking the diagnosis using both well-known diagnostic methods (prostate-specific antigen PSA, digital rectal examination, transrectal ultrasound, transrectal dopplerography of prostate vessels) and a new method - histoscopy. . During the work, a comparative analysis of standard research methods and diagnostic capabilities of histoscan for prostate cancer and hyperplasia was carried out. In addition, the diagnostic value of the method related to early detection of cancer, the accuracy of staging the process, and the impact of the obtained results on the planning of polyfocal prostate biopsy and the choice of subsequent treatment tactics were determined.

First of all, a retrospective group of patients (hereinafter referred to as the first group) was identified and examined - 67 patients with suspected prostate cancer underwent prostate biopsy from 2009 to 2011. He conducted a standard diagnostic complex for a patient with suspected prostate cancer, consisting of clinical and biochemical blood tests, detection of prostate specific antigen (total share and, according to the instructions, free (PSA total > 4 ng / ml), PSA density), general urinalysis, 3-cup test, uroflowmetry, transabdominal and transrectal ultrasound examination of the prostate gland,

as well as Doppler ultrasound examination of the vessels of the prostate gland, after which a transrectal polyfocal biopsy was performed.

Next, to directly address the goals and objectives of our study, we examined 701 patients using the Histoscan device. All these patients underwent the above-mentioned standard diagnostic complex. The distribution of prostate-specific antigen levels in them was from 1.09 to 209 ng/ml.

Patients with high PSA levels who underwent histoscopy were divided into 3 groups based on the degree of its increase. Thus, 67 patients (to compare the results of prostate biopsy with and without histoscopy) and two control groups were identified.

In the first four groups (patients with suspected prostate cancer), all patients underwent prostate biopsy.

With the introduction of Histoscan, every patient who came to our clinic with a high PSA level (or with a normal PSA level, but prostate cancer was suspected by other examination methods) was assigned to one of the above groups. Then, the patients were examined according to the scheme developed for this study. This was a classic examination of a patient with suspected prostate cancer. The first step was a digital rectal examination (DRE). Seven (1.5%) of 456 patients in the second group had suspicious areas for prostate cancer. In the third group of 112 patients, 17 (15.3%) DREs were suspicious for cancer. In the fourth group, during DRE, 63 out of 70 patients had suspicious areas, that is, 87.5% of patients in this group. In the fifth group - a conditional control group - none of the 20 patients had suspicious areas detected during digital rectal examination. In the sixth group, none of the subjects had suspicious areas during DRE.

In the first group of 67 patients, 15 (22.3%) had areas suspicious for prostate cancer during digital rectal examination (Table 2).

Identification of suspicious areas during DRE in patients of research groups.

After that, a classic gray ultrasound examination - transabdominal and transrectal examination was performed, after which a Doppler examination was performed. According to the examination data, the presence or absence of suspicious foci for prostate cancer was recorded (Figure 6). It should be mentioned here that we did not take into account the changes according to TRUS and Doppler data, which are characteristic of prostatitis and prostate adenoma.

In none of the 456 patients in the second group, we found changes characteristic of prostate cancer according to TRUS and Doppler examination of blood flow of prostate vessels. In the third group with PSA thresholds of 10-20 ng/ml, ultrasound signs of prostate cancer were not found in any of the patients, as in the second group. In the fourth group, 30 out of 70 patients, i.e. 43.8%, have ultrasound signs characteristic of prostate cancer. In the fifth group, TRUS and Doppler ultrasonography of the prostate gland did not reveal changes specific to prostate adenocarcinoma in any of the patients. No changes were found in the youth of the sixth (control) group.

In the first group of 67 patients, 11 had classic hypoechoic areas suspicious for prostate cancer, which is 16.4% of all patients in the group.

The second stage of the study was to conduct a histoscope with mapping of the prostate gland for biopsy. Histoscopy begins with transrectal ultrasound.

Transrectal ultrasound examination is performed in two projections: the prostate gland is shown in a transverse projection, then in a sagittal one. After that, the prostate gland is scanned in the sagittal plane. This is possible due to the fact that the sensor is mounted on a special magnetic coil that rotates 180 ° when it is in the rectum.

After that, the prostate ultrasound data is processed by HistoScan's device. During processing, histoscan creates three projections of the prostate gland. The first two: sagittal and transverse - are obtained by ultrasound scanning.

Prostate gland with construction of a 3D model in 3 projections.

Prostate gland in 3 projections and 3D model with histoscopy tissue (suspicious for prostate cancer) shown in green.

In the 3D model, histoscan tissue (suspicious for prostate cancer) is shown in green.

Then the device of HistoScan (hereinafter referred to as histoscan) based on these data, independently constructs the third, virtual plane of the prostate - frontal (cranial). Based on the information obtained from the three projections, the histoscan creates a 3D model of the prostate gland, which can be oriented in space as needed by the researcher.

After creating all the projections of the prostate gland and creating a 3D model, the researcher further defines the boundaries of the prostate, which he first independently defines. The prostate ultrasound data is then processed by the Histoscan device. Thus, in the 3D model, we obtained suspicious areas for prostate cancer. Then a map of the prostate gland was created for biopsy, where suspicious areas for prostate cancer were also marked.

In the third stage of the study, some patients with a high risk of cancer, that is, some patients in groups 3 and 4, underwent MRI with an endorectal coil, and several of them additionally underwent CT of the pelvic organs.

The fourth stage of the examination was transrectal polyfocal prostate biopsy under ultrasound control for patients of groups 2, 3 and 4 (groups 1, 5 and 6 - control).

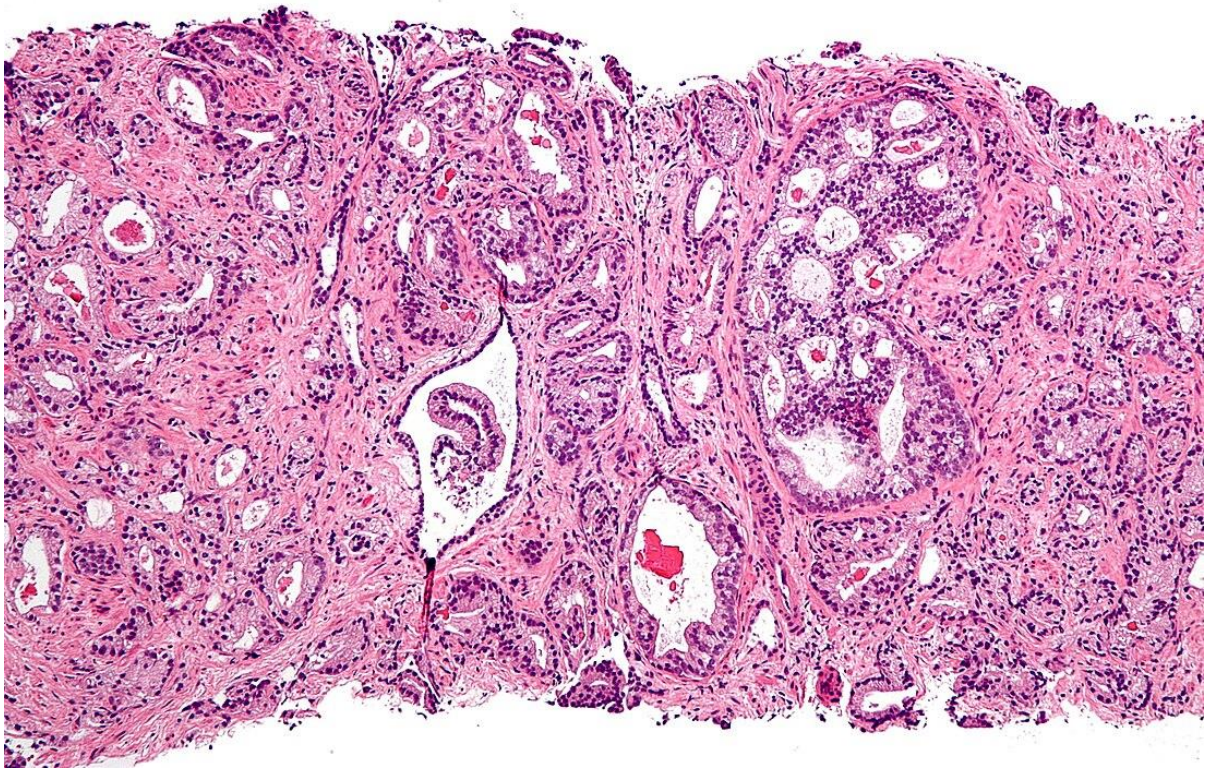
It should be noted here that, unlike the patients of the first group, in this case prostate biopsy was performed according to the maps of the prostate gland obtained by histoscanning. For the convenience of evaluating the results of the technique, each studied prostate gland is divided into 6 zones - sextants. Histoscan provides information in cubic centimeters on the volume of each of these sextants, as well as the volume of pathological tissue in a given sextant. The device then adds and displays the total volume of the gland, as well as the total volume of lesions that are suspicious for prostate cancer in the specific prostate gland being studied. This information, due to computer processing, is more accurate than the size of the gland measured during ultrasound examination.

It should be noted that the number of sextants for each patient is constant and equal to 6 (Figure 2). But the number of sites taken during the biopsy varied and depended on the size and number of suspicious sites according to histoscopy. Biopsies from these areas were considered suspicious. We evaluated the presence or absence of a suspicious lesion based on the histoscopic data in a certain sextant and then the morphological picture of this area - this is the first way to compare the histological examination data and the morphological conclusion. Morphological findings in the study were the gold standard for prostate cancer detection. Then, the data of all studies were compared with each other.

Sextants in the prostate gland.

Prostate sextants - sagittal projection on the left, cranial on the right (tissue suspected of prostate cancer is shown in pink)

Sagittal projection of the prostate gland on the left, cranial projection on the right. Pink in both projections indicates tissue suspicious for prostate cancer. Arrows in the cranial projection of the prostate indicate sextants.



Also, in order to optimize and simplify the calculation of patient examination results using histoscan, a second method for evaluating the sensitivity and specificity of histoscan was developed. First, we counted the number of tissue cores obtained from suspicious areas during polyfocal prostate biopsy for each patient and summed their number. These were standard sutures of tissue taken from suspicious areas and additional sutures taken from suspicious areas. For example, the total number of suspicious columns of prostate tissue in the second group of patients was 2684.

Second, in the same way, we calculated for each of these patients the number of tissue columns obtained during polyfocal prostate biopsies from areas that were not changed according to histoscan. The number of these prostate tissue columns was 3700. That is, the number of columns of non-suspicious prostate tissue was 3700. This number constitutes the standard column of prostate tissue.

Sampling scheme for tissue columns for prostate biopsy.

Sampling scheme for tissue columns for prostate biopsy

Map of the prostate gland, arrows indicate sites for additional tissue sampling during prostate biopsy. Thus, a total of 16 prostate tissue columns were obtained from this patient: 12 standard and 4 from suspicious sites.

Histoscan map.

Histoscan map - locations of additional columnar collections are indicated by arrows

Grid locations for additional posts are indicated by arrows.

Next, we evaluated the morphological picture in all columns of prostate tissue and compared it with the results of histoscan.

After receiving these data, we calculated the sensitivity and specificity of the prostate cancer detection method using the Histoscan device.

In addition to the above, we developed a third method to evaluate the morphological picture in suspicious areas according to histoscopic data, which consists in conducting an additional postoperative biopsy after radical prostatectomy, in which both suspicious areas and also taken from unchanged places. tissues according to histoscopic data. For this purpose, the removed gland is

specially marked in quadrants of 5 × 5 mm size. This feature made it possible to spatially correctly project suspicious areas from histoscopy data into the prostate gland. Having numbered the tissue columns, we sent them for morphological examination, which was carried out blindly, that is, the morphologists did not know which areas of the prostate they were examining (Figure 3).

Comparison of prostate mapping for blinded postoperative biopsy.

Photo of the removed prostate gland on the left, histoscopy map on the right

On the left is a photograph of the removed prostate gland (specially marked 5x5 mm), on the right is a map taken from a histoscan (also marked 5 × 5 mm).

The morphological study data were then compared with the histoscopy data. This comparison was made together with expert morphologists after radical prostatectomy. It should be noted here that there are several methods of postoperative evaluation of the prostate gland. We used the following method: first, the entire prostate was cut by a morphologist like an "open book": sections of the organ were made from the base to the apex with a 2-3 mm thick slice and were incomplete. end, that is, compared to an open book, the zone became "the binding of this book". The results of the morphological study fully confirm the histoscan data: according to the histoscan data, the node is macroscopically located in the right lobe, and during the morphological study, the node is adjacent to the prostate capsule in the right lobe (Fig. 5); .

Macroscopic specimen and prostate map.

A macroscopic sample of the prostate gland - part of the tumor tissue is surrounded by red color

A. Macroscopic preparation of the prostate gland in open-book view, with some tumor tissue circled in red.

Prostate schematic map - blue arrow indicates dashed line

B. Prostate map with dashed line indicated by blue arrow.

Thus, using histoscan data, 638 prostate biopsies were performed, their morphological findings were compared with the data of 67 prostate biopsies performed without histoscopic data, as well as with the data of 53 morphological studies after prostatectomy.

Results

More than 700 patients with suspected prostate cancer were examined by histoscopy.

It was found that during histoscopy, prostate cancer in the peripheral parts of the prostate gland is usually seen on a gray scale without suspicious foci, and the urethral zone is colored and it looks like this on the map made during histoscopy. prostate with a clear peripheral zone (grey), where in the central zone (projection area of the urethra) red or pink areas appear (false suspicious areas - a variant of the norm).

The following data were obtained when analyzing the possibilities of early diagnosis of prostate cancer using histoscopy. The majority of patients screened were patients with a baseline PSA level of less than 10 ng/mL. In the majority of patients in this category, none of the currently generally accepted noninvasive methods of diagnosing prostate cancer have provided information on the presence of suspected prostate cancer. The number of patients in this group was 456 or 64.3% of all examined patients. At the initial stage, we planned that the lower limit of the PSA level for this group would be 4 ng / ml, but during the study, we identified patients after histoscan examination, although the PSA level in the blood was normal (less than 4). ng/ml), prostate biopsy is indicated.

In patients with suspected prostate cancer, prostate biopsy was performed according to the prostate map obtained by histoscanner. The number of columns of prostate tissue obtained during biopsy is individual for each patient and varies depending on the size and number of suspicious areas for prostate cancer according to histoscan data. As a rule, during transrectal biopsy, we collected 12 conventional tissue columns and one or more columns in addition to them, depending on the presence of suspicious areas according to histoscanning data.

It should be noted that in 317 patients of the second group (patients with suspected prostate cancer with a PSA level of up to 10 ng/ml) during the classic polyfocal biopsy of the prostate gland, according to histoscopic data, suspicious areas, completely prostate to fell to sampling sites. Accordingly, we did not obtain additional columns from these patients, and standard columns of prostate tissue from suspicious sites were marked as suspicious by us.

But in the remaining 139 patients in the second group, suspicious areas during standard biopsies were partially or completely not included in the tissue sampling sites. These patients had additional cores obtained during prostate biopsy that were marked as suspicious. Thus, a total of 6384 columns of prostate tissue were obtained for all patients of the second group, of which 3804 were standard columns and 2580 were additional columns of prostate tissue.

The following method was developed to optimize and simplify the calculation of patient examination results using Histoscan. First, we counted the number of tissue cores obtained from suspicious areas during polyfocal prostate biopsy for each patient and summed their number. These were standard sutures of tissue taken from suspicious areas and additional sutures taken from suspicious areas. The total number of suspicious columns of prostate tissue in the second group of patients was 2684. Second, for each of the same patients, the number of tissue columns obtained during polyfocal biopsy from unaffected areas of the prostate according to histoscopic data was calculated. the same. The number of these prostate tissue columns was 3700. That is, the number of columns of non-suspicious prostate tissue is 3700. This number is the standard column of prostate tissue.

Next, we evaluated the morphological picture in all columns of prostate tissue and compared it with the results of histoscan.

When comparing the results, the following information was obtained. Of the 2,684 prostate tissue samples taken from suspicious sites, 2,389 were found to have prostate cancer. Of 2,684 suspected, high-level PINs, 157 were morphologically identified in prostate tissue. Of the 2,684 suspicious columns, 138 columns were labeled "no cancer or stage III PIN."

Also, out of 3700 non-suspicious columns of prostate tissue, we found prostate cancer in 22 years.

After obtaining these data, we calculated the sensitivity and specificity of the histoscan method in early detection of prostate cancer. The total number of prostate columns obtained during biopsy from all patients in the second group was 6384. The number of prostate columns with suspicious areas during histoscopy was 2684. detected during histoscopy, in which cancer was confirmed according to morphology, was 2389.

Accordingly, statistical processing was established: sensitivity of histoscan in early diagnosis of prostate cancer is 89%, specificity is 96%.

During histoscopy, suspicious areas were identified, the number of prostate tissue columns with a high-level PIN code according to their morphology was 157. Of this, the false positive result of histoscanning was determined, which was 11%. and the false negative result was 0.6%.

Also, in cooperation with morphologists, a method of macroscopic diagnosis during morphological examination was developed. We have developed a technique for counting sextants in the prostate. When mapping the prostate after histoscopy, sextants were obtained when the glands were automatically divided into 6 zones. Accordingly, the total number of sextants for the second group is determined by the following formula: the number of patients in the group is multiplied by six ($456 \times 6 = 2736$).

For each patient, in addition to the evaluation of tissue columns, the results of histoscopy of the prostate gland were evaluated using sextants, that is, we evaluated the map of the prostate, where suspicious areas for prostate cancer were drawn. In each specific case, the number of sextants affected was determined, and then the morphological picture in these sextants was compared.

Later, after prostate biopsy, in collaboration with expert morphologists, correspondence was established between the location of the tumor focus according to histoscan data and the morphological study of prostate tissue biopsies.

The following information was obtained. In the second group, 456 studies were conducted in patients whose PSA level rose to 10 ng/ml. The total number of sextants for the second group is 2736 (6 × 456 = 2736). Out of the total number of sextants, 1642 are sextants where suspicious areas have been identified based on histoscopy data. A positive result was obtained in 1445 sextants in the evaluation of morphological data. That is, according to the results of histoscopy, prostate cancer was morphologically confirmed in 1445 out of 1642 sextants with suspicious areas. Thus, the sensitivity of the histoscan in the second group using sextant evaluation in the statistical processing of the obtained data confirms the sensitivity data in the evaluation of biopsy cores and is equal to 88%.

Analyzing the data obtained after the morphological evaluation of histoscopy results, we first determined our data on the sensitivity and specificity of the histoscanning technique. The sensitivity of the histoscopy technique in early diagnosis of prostate cancer was 88%, and the specificity was 96%. Our data confirm European data and clearly show that histoscopy is the most effective non-invasive method for early diagnosis and localization of prostate cancer. Histoscan also allows you to plan a biopsy, create a map of the prostate gland, and then plan your treatment. According to our data, histoscopy is very effective in detecting lesions suspicious for prostate cancer in their early stages. At these stages, neither digital rectal examination nor ultrasound data - TRUS and Doppler sonography provide such information about the prostate tumor.

Patients with low cancer risk and localized prostate cancer underwent radical prostatectomy. After radical prostatectomy, in close cooperation with expert morphologists, the results of histoscopy were evaluated and compared with the results of pathological examination of the organ. We have put into practice the technique of blind biopsy of the prostate after surgery. The essence of the technique is that the gland removed after radical prostatectomy is specially marked into quadrants measuring 5 × 5 mm. Later, according to the prostate map, a postoperative biopsy was performed. During biopsy, areas suspicious for prostate cancer according to histoscopy and unaffected by histoscopy were removed. Having numbered the tissue columns, they were sent to a morphological study, which was performed blindly, so 53 comparisons were made. Macroscopic concordance of prostate cancer with histoscopic data was found in 2 cases. I would like to note here that macroscopically, prostate cancer areas are rarely visible. According to the postoperative biopsy, it was found that the histoscopic data corresponded to the morphological research data in 88% of cases, which further confirms our data on the sensitivity and specificity of the technique in the first group of patients.

Later, by analyzing the data obtained after the morphological evaluation of histoscopy results in the third group of patients, we obtained data on the sensitivity and specificity of the histoscanning technique. For patients in the third group, the sensitivity of the histoscopy technique in diagnosing prostate cancer was 96%, and the specificity was 97%. We can also compare the sensitivity and specificity of histoscanning and magnetic resonance imaging. Histoscopy is superior to existing non-invasive methods for diagnosing prostate cancer.

After the morphological evaluation of histoscopy results in the fourth group of patients, we obtained information about the sensitivity and specificity of the histoscanning technique. In patients of the fourth group, the sensitivity of the histoscopy technique in diagnosing prostate cancer was 99%, and the specificity was 97%. We can also compare the sensitivity and specificity of histoscanning and magnetic resonance imaging.

I would like to emphasize that the first group of patients was determined to evaluate the effectiveness of prostate biopsy without histoscanning and without using histoscanning - a retrospective evaluation. Thus, the effectiveness of prostate biopsy without histoscopy was 50%, with the help of histoscopy it increased by 22% and reached 72%, respectively.

Thus, our data (Table 4) confirm European data and clearly show that histoscopy is the best non-invasive method for early diagnosis and localization of prostate cancer [5].

Summary

Thus, usually on the histoscopy map, the prostate gland is presented as a prostate with a clear peripheral zone (gray), where red or pink areas appear in the central zone (projection area of the urethra). On the histoscopy map, prostate cancer is red or pink colored areas, the total volume of which exceeds 0.2 cm^3 in one sextant. Staining of the urethral area does not indicate the presence of prostate cancer. Histoscopic map with prostatic hyperplasia shows colored areas in the urethral zone (normal variant), and small scattered colored areas appear on the sextant, the total volume of which does not exceed 0.2 cm^3. When the clinical and morphological comparison of the results of histoscopy and morphological examination data was determined, in 91% of cases it was found that the localization and size of prostate cancer foci were completely consistent. Histoscan has a sensitivity of 88% and a specificity of 96% for detecting prostate cancer in patients with a PSA level of 4 to 10 ng/ml; In patients with a PSA level of 10 to 20 ng/ml, sensitivity of histoscan is 96%, specificity is 97%; In patients with PSA above 20 ng/ml, sensitivity is 99%, specificity is 97%. The information content of a prostate biopsy using histoscan data is 22% higher than without prior mapping of the prostate gland with a histoscope. Histoscopy is an additional non-invasive method for early diagnosis of prostate cancer, which allows to increase the information content of prostate biopsy and is not intended to evaluate the extracapsular spread of prostate cancer, the state of paraprostatic tissue and regional lymphadenopathy.

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