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Research Article

# Mathematical Method For Determining The Critical Size Of A Lymph Node Using Ultrasonography.

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**Abstract**

The paper investigates the values of the patient's lymph nodes measured by ultrasonography in order to determine such a critical value that would exclude the actual size of the gland exceeding the given value, which is necessary for a reliable selection of the treatment method. The uniformity of the arithmetic means and variances of the random component of the observation groups is established. Also, their probability distribution is in accordance with the normal law. Using this, a critical value for the size of a patient's lymph node measured by ultrasonography has been obtained - when the measured value of the node does not exceed it, a decision is made with a given reliability that the lymph node size is below the critical value.

**Keywords** : lymph node; ultrasonography; computed tomography; Bartlett's criteria; Fisher's criteria; Kolmogorov-Smirnov test.

## INTRODUCTION

Determining the size of the patient's lymph nodes is an important moment for choosing a treatment method. For this purpose, ultrasonography and computed tomography methods are used, the first of which has less accuracy and low price, and the second has high accuracy and increased price. In addition, the first method is more widespread and, therefore, more accessible to the patient than the second. The computed tomography method, due to its accuracy, is considered a certain standard, based on the results of which the final decision on treatment is made.

It is known that if the size of the gland exceeds the critical value $C=5$, radical treatment measures must be used. From the above, it is clear that when determining the size of the lymph nodes by ultrasonography, it is very important to exclude cases where the size of the gland is taken to be less than the critical value, while in reality it exceeds this value.

The aim of the study below is to determine the threshold value of the measured value when determining the size of the lymph gland by ultrasonography, below which, for the obtained measurement values, we can conclude with a given probability that the real (true) value of the gland does not exceed the critical size $C$.

The research results are presented in the paper as follows: the results of the formalization of the problem under consideration and the preliminary study of the data are given in Section 2; the method for determining the critical size of the lymph gland is presented in Section 3; a brief conclusion is given in Section 4.

## PROBLEM FORMALIZATION AND PRELIMINARY DATA ANALYSIS

**Table 1** shows the lymph node sizes measured by ultrasonography and computed tomography for 55 patients[1]. To achieve the set goal, we proceed as follows. Since both methods measure the same quantity and the results obtained

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by the computed tomography method are much more accurate than those obtained by the ultrasonography method, we can assume that the result obtained by the computed tomography represents the mathematical expectation of the result obtained by the ultrasonography method. Let $x_i, m_i, i=1,...,n$ be the measurement results obtained by the ultrasonography and computed tomography methods, respectively, i.e. we can write that the mathematical expectation $E(xi)=mi, i=1,...,n$. Let us calculate the random components of the measurement results obtained by the ultrasonography method, i.e. $\varepsilon_i=x_i-m_i, i=1,...,n,$ and examine them. In **Table 1,** the measurement results are grouped according to the size of the lymph gland. The first group contains the measurement results when the gland size (obtained by the computed tomography method) is practically zero. For the second group, the gland size is between 0 and 2, for the third group - between 2 and 5, and for the fourth group - above 5. Let us examine these groups for homogeneity, i.e. determine whether the mathematical expectation and variance of the random component (i.e. of $\varepsilon_i$) of the ultrasonography method change according to the groups[2]. This will allow us to determine whether the measurement accuracy depends on the size of the gland. To determine the homogeneity of the variance and mathematical expectation of the mentioned random component, we use Bartlett's and Fisher's criteria, respectively, the essence of which is as follows (Primak et al., 1991; Kendall and Stuart, 1966):

**Table 1.** Lymph node sizes measured by ultrasonography and computed tomography.

| № | Groups (gland size intervals) | Ultrasonography (US) | Computed tomography (CT) |
|---|---|---|---|
| 1-4 | N_0 (0÷1) | 0, 1.5, 1.5, 1.3 | 0, 0, 0, 0 |
| 5-19 | N_1 (1÷2.3) | 2.3, 1.5, 1.4, 1.5, 1.8, 1.2, 1.0, 1.5, 1.5, 1.7, 0, 0, 0, 0, 0 | 1.8, 1.8, 1.7, 1.5, 1.5, 1.5, 1.3, 1.7, 1.6, 1.6, 1.8, 0.7, 1.5, 0.8 ,1.2 |
| 20-32 | N_2 (2.3÷4) | 5.1, 5.2, 5.4, 4.5, 3.5, 3.2, 2.8, 2.5, 2.5, 1.8, 1.5, 0, 0 | 4.6, 4.8, 4.8, 4.5, 4.5, 4.0, 3.5, 2.8, 3.0, 3.2, 2.7, 2.5, 2.2 |
| 33-55 | N_3 (4÷23) | 4.5, 4.2, 4.8, 3.4, 13.0, 14.0, 10.0, 12.0, 8.5, 8.0, 8.0, 6.0, 7.5, 7.5, 5.5, 6.5, 5.7, 6.0, 5.5, 5.3, 6.0 ,5.0, 5.0 | 5.3, 6.2, 5.4, 5.2, 15.4, 13.7, 11.5, 10.8, 9.7, 8.5, 8.2, 7.8, 7.6, 7.2, 6.9, 6.5, 6.5, 5.4, 6.0, 5.8, 5.4, 5.0, 5.2 |

[1]The authors would like to thank Mr. Z. Mezvrishvili, a doctor at Tbilisi Hospital #1, for the task set and for providing the experimental data to solve it.

[2]The calculations in the paper were performed using the universal applied software package for processing experimental data, SDpro, created under the supervision of the author and, also, software SPSS (Bühl and Zöfel, 2001; Kachiashvili, 2018).

Calculate the averaged variances of the groups

$$S_{med}^2 = \frac{1}{n-L}\sum_{i=1}^{L}\left(n_i-1\right)\cdot S_i^2$$

where $n_i$ is the number of observations in the $i$th group, $n$ is the total number of observations $n=\sum_{i=1}^{L} n_i$; $L$ is the number of observation groups; $S_i^2$ is the $i$th group variance

$$S_i^2 = \frac{1}{n_i-1}\sum_{j=1}^{n}\left(x_{ij}-\bar{x}_i\right)^2$$

$x_{ij}$ is the $j$th element of the $i$th group of observations, $x_i$ is the arithmetic mean of the ith group.

Statistics

$$\chi^2 = \frac{2.303}{D}\left[\left(N-L\right)\ln S_{med}^2 - \sum_{i=1}^{L}\left(n_i-1\right)\ln S_i^2\right]$$

where

$$D = 1+\frac{1}{3\left(L-1\right)}\left(\sum_{i=1}^{L}\frac{1}{n_i-1}-\frac{1}{N-L}\right)$$

obeys the distribution law $\chi^2$ with degrees of freedom equal to $(L\text{-}1)$.

According to Bartlett's criterion, if the condition

$\chi^2_{\alpha/2} \le \chi^2 \le \chi^2_{1-\alpha/2}$ holds, where $\chi^2_{\alpha/2}$ and $\chi^2_{1-\alpha/2}$ are the quantiles of the level $\alpha/2$ and $1\text{-}\alpha/2$ according to the distribution law $\chi^2$ with degrees of freedom equal to $(L\text{-}1)$, a decision is made about the homogeneity of the variances of the observation groups with a confidence probability equal to $1\text{-}\alpha$.

**Table 2** presents the statistical characteristics of the random variables of the measurement results obtained by the ultrasonography method, calculated using SPSS (Bühl and Zöfel, 2001).

**Table 2.** Statistical characteristics of random components of measurement results obtained by the ultrasonography method.

| Statistics | | | | | |
|---|---|---|---|---|---|
| **N** | **x1y1** | **x2y2** | **x3y3** | **x4y4** | **AllxAlly** |
| Valid | 4 | 15 | 13 | 23 | 55 |
| Missing | 51 | 40 | 42 | 32 | 0 |
| Mean | 1.0750 | -.4400 | -.7000 | -.5783 | -.3673 |
| Median | 1.4000 | -.3000 | -.7000 | -.5000 | -.2000 |
| Mode | 1.50 | -.30 | -2.50a | -.50 | .00 |
| Std. Deviation | .72284 | .65005 | .97297 | .92979 | .92937 |
| Variance | .523 | .423 | .947 | .865 | .864 |
| Skewness | -1.902 | -.800 | -.431 | -.205 | -.289 |
| Std. Error of Skewness | 1.014 | .580 | .616 | .481 | .322 |
| Kurtosis | 3.634 | .083 | -.461 | -.560 | .004 |
| Std. Error of Kurtosis | 2.619 | 1.121 | 1.191 | .935 | .634 |

a. Multiple modes exist. The smallest value is shown

Here, the statistical characteristics of the random components of the corresponding groups are denoted by $x_i y_i, i=1,...,4$, and the statistical characteristics of the combined groups of random components are denoted by *AllxAlly*. From this, we can easily find that $S^2_{med}$=0.7428 and the statistics $\chi^2$=5.8178. The range of acceptance of the hypothesis of homogeneity is [0.2158; 9.3484] with a confidence probability of 0.95. From this we conclude that with a confidence level of 0.95, the variances of the observation groups are homogeneous, that is, the measurement accuracy does not depend on the size of the gland.

The homogeneity of the variances of the groups allows us to use Fisher's test to check the homogeneity of the mathematical expectations of the groups, the essence of which is as follows. Calculate the estimate of the intergroup variance

$$S^2_{\Sigma L} = \frac{1}{L-1}\sum_{i=1}^{L} n_i\left(\bar{x}_i - \bar{\bar{x}}\right)^2$$

and the average value of the variances in the groups

$$S^2_{nL} = \frac{1}{n-L}\sum_{i=1}^{L}\sum_{j=1}^{n}\left(x_{ij} - \bar{x}_i\right)^2$$

where

$$\bar{\bar{x}} = \frac{1}{n}\sum_{i=1}^{L}\sum_{j=1}^{n} x_{ij} = \frac{1}{n}\sum_{i=1}^{L} n_i \cdot \bar{x}_i$$

is the arithmetic mean of the total number of observations.

It is known that the ratio $S^2_{\Sigma L}/S^2_{nL}$ obeys the Fisher distribution law $F_{k1,k2}$ with degrees of freedom equal to $k_1=L-1$ and $k_2=n-L$ (Primak et al., 1991; Kendall and Stuart, 1966). Therefore, if the inequality $F_{\alpha/2} \le S^2_{\Sigma L}/S^2_{nL} \le F_{1-\alpha/2}$ holds, where $F_{\alpha/2}$ and $F_{1-\alpha/2}$, are the α/2 and 1-α/2 level quantiles of the Fisher distribution law with degrees of freedom equal to $k_1$ and $k_2$, a decision is made on the homogeneity of the arithmetic means of the groups. Thus, for the critical values $F_{\alpha/2}$ and $F_{1-\alpha/2}$ the condition is satisfied

$$P\left(F_{\alpha/2} \le S^2_{\Sigma L}/S^2_{nL} \le F_{1-\alpha/2}\right) = 1-\alpha$$

where 1-α is the probability of confidence in the criterion.

From the data given in Table 1 it can be seen that for the first group, for which the size of the gland is practically zero, the results obtained by the ultrasonography method are quite rough. Since the data of the first group have no influence on the solution of the problem posed, we will check the uniformity of the arithmetic means only for the second, third and fourth groups. In this case, for the above statistics we obtain: $S^2_{\Sigma L}$=1.2711 and $S^2_{nL}$=0.7566. Their ratio is $S^2_{\Sigma L}/S^2_{nL}$=1.68. The area of acceptance of the hypothesis of homogeneity of mathematical expectations of groups is [0.0253; 3.9875] with a confidence probability 1-α=0.95, i.e. we conclude that with a confidence probability of 0.95 the mathematical expectations of the random components of the ultrasonography method are homogeneous in the last three observation groups. This allows us to conclude that if the ultrasonography and computed tomography methods had a constant component of measurement error, it would be constant over the entire measurement range.

## DETERMINATION OF THE CRITICAL SIZE OF THE LYMPH GLAND

Since $\varepsilon_i, i=5,...,55$, are uniform in the entire measurement range both in terms of mathematical expectations and variances, it is possible to combine them for study as homogeneous groups of observations. That is, the condition holds that $\varepsilon_i, i=5,...,55$, are the results of observations on the same random variable, the mathematical expectation and variance of which are equal to $E(\varepsilon)=m$ and $V(\varepsilon)=\sigma^2$, respectively. To solve the above problem, it is necessary to determine the law of distribution of the random variable ε. To make a decision $\chi^2$, the Kolmogorov-Smirnov and $\omega^2$ criteria were used (Kendall and Stuart, 1970). The $\chi^2$ criterion has the following form. Suppose we want to test the hypothesis that a random variable $\varepsilon$ obeys the law of probability distribution with density $f(x)$. The quantity is calculated

$$\chi^2 = \sum_{i=1}^{k} \frac{\left(P_i - P_i^*\right)^2}{P_i}$$

where $k$ is the number of intervals of the random variable; $P_i$ is the frequency of falling into the ith interval calculated from the observation results; $P_i^*$ is the probability of falling into the $i$th interval calculated from the density of the distribution $f(x)$. If the inequality

$$\chi^2_{v;\alpha/2} \le \chi^2 < \chi^2_{v;1-\alpha/2}$$

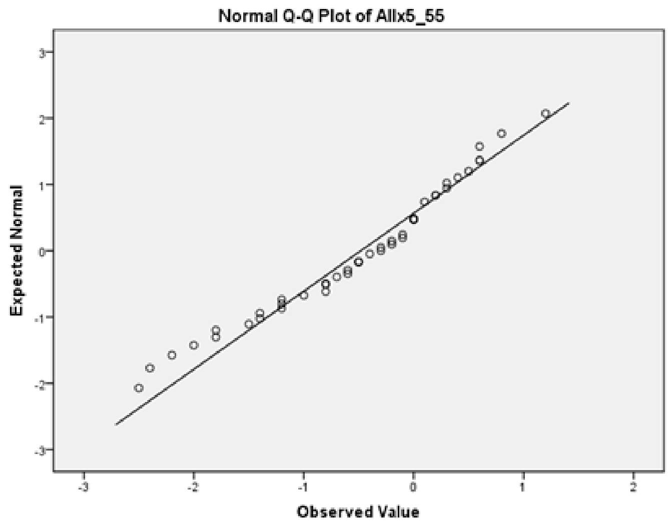
takes place, where $\chi^2_{v;\alpha/2}$ and $\chi^2_{v;1-\alpha/2}$ are the α/2 and 1-α/2 level percentage points of the $\chi^2$ distribution law with degrees of freedom $v=k-\mu-1$, then it is decided that the random variable under investigation obeys the distribution law $f(x)$;$\mu$ is the number of unknown parameters of the probability distribution density $f(x)$.

To determine the distribution law of the random variable $\varepsilon$, the normal, uniform, triangular, trapezoidal, truncated Rayleigh and Student distribution laws were investigated (Primak et al., 1991). All the above criteria showed that the random component of the ultrasonography method obeys the normal distribution law with a confidence probability of 0.95. In particular, in the case under study, the following conditions were met:

1. The value of the statistic for criterion $\chi^2$ is equal to $\chi^2$=1.0275. The range of acceptance of the hypothesis is [0.2158; 9.3484] with a confidence probability of 0.95. That is, according to the criterion $\chi^2$, the random variable $\varepsilon$ obeys the law of normal distribution with a confidence probability equal to 0.95.
2. The value of the corresponding statistic for the Kolmogorov-Smirnov criterion is equal to $D_N$=0.9726. The range of acceptance of the hypothesis is [0.4806; 1.4802] with a confidence probability of 0.95. That is, according to the Kolmogorov-Smirnov criterion, the random variable $\varepsilon$ obeys the law of normal distribution with a confidence probability equal to 0.95.
3. The value of the statistic corresponding to the criterion $\omega^2$ is equal to $\omega^2$=0.1797. The range of acceptance of the hypothesis is [0.0304; 0.5806] with a confidence probability of 0.95. That is, the mentioned criterion also agrees with the hypothesis, according to which the random variable $\varepsilon$ obeys the law of normal distribution with a confidence probability equal to 0.95.

It is known that the considered universal tests of goodness of fit cannot provide a high level of significance for a small number of observations. Therefore, to test the normality of the distribution law of the random component of the ultrasonography method, we will use another - graphical method, which, despite its simplicity, gives reliable results even for a small number of observations (Kachiashvili and Nurani, 2013). The result of using this method is given in **Figure 1**, from which it is clearly seen (the observation results fit quite well on the line) that the observation results are distributed according to a normal law.

**Figure 1.** Graphical method of examination of the probability distribution of the random component of measurement results obtained by the ultrasonography method for normality.




Thus, we have obtained that the random component of the measurement results obtained by the ultrasonography method obeys the law of normal distribution with probability density $N(x;m,\sigma^2)$. In order to find a size that we can compare with the measurement result obtained by the ultrasonography method and if this result turns out to be less than the specified size $C$, then the probability that the true size of the gland does not exceed the value of $C$ will be equal to $1-\alpha$, we need to solve the equation

$$\int_{-\infty}^{C} N\left(x;m,\sigma^2\right)dx = 1-\alpha$$

with respect to $m$.

As mentioned above, there is a condition

$$N\left(x;m;\sigma^2\right) = \frac{1}{\sqrt{2\pi}\cdot\sigma}\exp\left\{-\frac{\left(x-m\right)^2}{2\sigma^2}\right\}$$

Taking this into account, solving the integral equation gives us

$$m=C-\sigma.\Phi^{-1}(1-\alpha), \qquad (1)$$

where $\Phi^{-1}(\cdot)$is the inverse function of the standard normal distribution.

The estimate of the mean square deviation for the observation results given in Table 1 is $\hat{\sigma}$=0.8497. Using the statistical software package SPSS, we find (Bolshev and Smirnov, 1983):

$\Phi^{-1}(0.95)=1.6449$, $\Phi^{-1}(0.98)=2.0537$, $\Phi^{-1}(0.99)=2.3263$, $\Phi^{-1}(0.999)=3.0902$.

Thus, we obtained the following result: if the size of the gland measured by ultrasonography is less than or equal to the value of $m$ calculated by (1), then with a confidence probability equal to 1-$\alpha$, we conclude that the size of the gland does not exceed $C$.

For $C$=5 we get : $m_{0,95}$=3.6023; $m_{0,98}$=3.25497; $m_{0,99}$=3.02334; $m_{0,999}$=2.37425.

If we compare the obtained results with the data given in Table 1, we will see that in only one case the measurement result obtained by the ultrasonography method, 3.4, is less than $m_{0,95}$=3.6023, that is, the decision is made that the size of the gland is less than 5, when the actual size of the gland is 5.2, which exceeds $C$=5. However, if we increase the probability of confidence in the decision and take equal to or higher than 1-α = 0.98, the mentioned error will also be eliminated. It is also worth noting that the number of reverse errors made during decision-making, i.e., the erroneous decision that the size of the gland exceeds the critical value, is equal to 4 at a confidence probability of 0.95, and this number increases with increasing confidence probability. The presence of such errors in solving the problem posed is not critical, since it does not have a negative impact on the patient’s health, it is associated only with additional costs incurred by the patient, which is quite acceptable for the purpose of health protection.

## CONCLUSION

The paper proposes a method for determining critical values for the patient’s lymph node sizes obtained by ultrasonography, in order to exclude with a selected probability the possibility of the actual size of the gland exceeding a given value $C$, for reliable selection of the treatment method.

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