

**CLINICAL EVALUATION REPORT - SUMMARY**  
**in Regards to the Progress of Clinical Trial Approved by**  
**Ethics Committee for Clinical Investigation of Medical Device**  
**with Statement № EKKM / CT – 0687 / 06.08.2020**

## **1. General information**

- Title of the clinical trial: Clinical presentation of CoLumbo software
- Main researcher: Assos. Prof. Dr. Radoslav Georgiev
- Clinical trial centers:
  1. St. Marina University Hospital – Varna;
  2. Dr. Stefan Cherkezov Hospital – Veliko Tarnovo;
  3. Pirogov Hospital – Sofia;

The medical device is Class IIa according to EU MDD 93/42, Annex IX, Rule 10.

## **2. Diagnostic Claims**

Pathologies supported by CoLumbo for detection:

- Disk herniation (without sequestration);
- Disk bulging;
- Central spinal stenosis;
- Nerve root impingement;
- Reduced vertebral height;
- Reduced disk height;
- Increased aortic diameter;
- Hypo- and hyperlordosis;
- Spondylolisthesis and pseudolisthesis;

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### 3. Results

These are the final results based on all 382 studies.

The mean value and the standard deviation of the ages of the patients were calculated to be:

- Average patient age: 49.52
- Standard deviation of age: 13.20
- Total number of studies: 382; Females 53.4%; Males 46.6%

The MRI acquisitions were conducted on 4 different machines, 3 different models (one of the models was present in 2 centers) from 2 different manufacturers:

Manufacturer	Model	Magnetic Field Strength
SIEMENS	Aera	1.5
GE MEDICAL SYSTEMS	Signa HDxt	1.5
SIEMENS	Verio	3.0

MR Acquisition Type - 2D and 3D

#### Statistics for the axial slices:

- Max Echo Time: 125
- Min Echo Time: 86
- Max Repetition Time: 6000
- Min Repetition Time: 2200
- Max Rows: 512
- Min Rows: 192
- Max Cols: 512
- Min Cols: 276
- Max Slice Spacing: 5.0
- Min Slice Spacing: 3.45

#### Statistics for the sagittal slices:

- Max Echo Time: 300
- Min Echo Time: 75

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- Max Repetition Time: 6000
- Min Repetition Time: 550
- Max Rows: 888
- Min Rows: 384
- Max Cols: 512
- Min Cols: 384
- Max 2D Slice Spacing: 5.0
- Min 2D Slice Spacing: 3.45
- Max 3D Slice Spacing: 0.9
- Min 3D Slice Spacing: 1.1

All in all, there were 156 debatable cases (disagreements between radiologists, using the software, and radiologist, not using the software) for the presence of central stenosis. In 18 cases the consensual or predominant opinion has coincided with that of a radiologist not using the software. In 138 cases the former has coincided with that of a radiologist using the software Columbo. Data is presented in table 2.

Diagnosis	Agreement between the opinions of a radiologist arbiter and a radiologist not using the software [%]	Agreement between the opinions of a radiologist arbiter and a radiologist using the software [%]	Difference [%]
Presence of central spinal stenosis	50%	50%	0%

Table 1

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<b>Diagnosis</b>	Agreement between the opinions of a radiologist arbiter and a radiologist not using the software [number of cases and % in brackets]	Agreement between the opinions of a radiologist arbiter and a radiologist using the software [number of cases and % in brackets]	Difference [number of cases and % in brackets]	p-value
Presence of central spinal stenosis	18(11.54%)	138(88.46%)	120(76.92%)	< 0.000001

Table 2

In order to prove that the difference in the level of agreement with the radiologist arbiter of a radiologist with the software compared to a radiologist without the software in the cases of disagreement is not worse than the one pointed out in column “Difference”(equivalently agreement between the opinions of a radiologist arbiter and a radiologist using the software is not worse than 50%) in tables 1 and 3, the following figures were calculated and recorded in tables 2 and 4.

<b>Diagnosis</b>	Agreement between the opinions of a radiologist arbiter and a radiologist not using the software [%]	Agreement between the opinions of a radiologist arbiter and a radiologist using the software [%]	Difference [%]
Herniation presence (without sequestration)	50%	50%	0%
Spondylolisthesis presence	50%	50%	0%
Bulging presence	50%	50%	0%
Hypolordosis presence	50%	50%	0%

Table 3

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Diagnosis	Agreement between the opinions of a radiologist arbiter and a radiologist not using the software [number of cases and % in brackets]	Agreement between the opinions of a radiologist arbiter and a radiologist using the software [number of cases and % in brackets]	Difference [number of cases and % in brackets]	p-value
Herniation presence (without sequestration)	132(43.14 %)	174(56.86%)	42(13.73%)	0.009470
Spondylolisthesis presence	9(30.00%)	21(70.00%)	12(40.00%)	0.021387
Bulging presence	199(41.29%)	283(58.71%)	84(17.43%)	0.000076
Hypolordosis presence	45(30.00%)	105(70.00%)	60(40.00%)	<0.000001

Table 4

Table 5

Diagnosis	Sensitivity [%]	Specificity [%]
Herniation presence (without sequestration)	65.00%	90.00%
Nerve root impingement grade when a herniation is presence	71.00%	90.50%
Dural sac compression, caused by herniation	76.00%	90.00%
Herniation position*	68.00%	N/A
Herniation migration (without sequestration)	75.00%	84.00%
Bulging presence	60.00%	92.00%
Central spinal canal stenosis presence	81.00%	90.00%
Spondylolisthesis presence	60.00%	88.00%
Spondylolisthesis grade*	89.34%	N/A
Pseudolisthesis presence	66.00%	90.00%
Hypo- and hyperlordosis presence /accentuated and straightened lordosis	75.00%	87.00%
Precise determination of levels*	90.00%	N/A

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\* For the Herniation position, Spondylolisthesis grade and Precise determination of levels accuracy are calculated instead of sensitivity and specificity as there are no positives and negatives but only matches and mismatches.

The following table aims at showing both the sensitivity in the high sensitivity mode and specificity in the high specificity mode. The above-listed table portrays the data only for sensitivity and specificity.

In high specificity mode, a 75% probability threshold for the presence of pathology was used. In high sensitivity mode, a 25% probability threshold was used.

<b>Diagnosis</b>	<b>Sensitivity in high sensitivity mode [%]</b>	<b>Specificity in high specificity mode [%]</b>
Herniation presence (without sequestration)	77.00%	94.00%
Nerve root impingement grade when herniation is present	77.00%	92.00%
Dural sac compression, caused by herniation	82.00%	92.00%
Herniation migration (without sequestration)	82.00%	91.00%
Bulging presence	70.00%	95.00%
Central spinal canal stenosis presence	86.00%	93.00%
Spondylolisthesis presence	75.00%	94.00%
Pseudolisthesis presence	81.00%	96.00%
Hypo- and hyperlordosis presence / accentuated and straightened lordosis	85.00%	92.00%
Precise determination of levels*	N/A	N/A

Table 6

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The table below depicts the average sensitivity and specificity of CoLumbo for the five pathologies obtained from the performed clinical trials. The factors which are being taken into consideration here are the gender and the age of the patients. Also, a separation between the different hospitals is being listed as well.

	Average sensitivity of the software for the five main pathologies derived from clinical trials	Average sensitivity of the software for the five main pathologies derived from clinical trials
Male patients	86.7%	95.72%
Female patients	82.51%	96.23%
Age group 1 (under 50 years old)	84.17%	96.45%
Age group 2 (50 years old and older)	85.76%	95.65%
Centre UMBAL Sveta Marina	83.03%	96.35%
Centre MOBAL DR STEFAN CHERKEZOV	77.55%	96.14%
Centre UMBALSM Pirogov	84.80%	95.69%

Table 7

To prove that the accuracy of the segmentation algorithm (in % measured key points with deviation below clinical significance) is not worse than the accuracy mentioned in table 8 below, the results in table 9 were calculated.

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The following table shows the accuracy of the different segmentations, that the CoLumbo software performs in its current version.

Segmentations	Accuracy [%]
Vertebra (on axial slice)	82.00%
Disk – not herniated (on axial slice)	87.00%
Herniated part of the disk, without sequestration (on axial slice)	85.00%
Dural sac (on axial slice)	84.00%
Ligamentum flavum (on axial slice)	80.00%
Nerve roots (on axial slice)	78.00%
Aorta or iliac artery (on axial slice)	88.00%
Vertebra (on sagittal slice, only around mid-sagittal, 35 mm)	81.00%
Disk – not herniated (on sagittal slice, only around mid-sagittal, 35 mm)	91.00%
Sacrum (on sagittal slice)	87.00%
Appropriately chosen planes*	70.00%

Table 8

The accuracy of the measurement algorithm (in % measured with deviation below clinical matter) with the help of the device is shown in Table 18.

The below-listed table represents the accuracy percentage of all the measurements which the CoLumbo software detects.

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Measurements	Accuracy [%]
Intervertebral angles, °	90.0%
L1S1 lordotic angle, °	86.0%
Percentage spondylolisthesis slippage	90.0%
Vertebral height, mm	78.0%
Disk height, mm	82.0%
Herniation size, mm	78.0%
Dural sac area, mm <sup>2</sup>	81.0%
Aorta diameter, mm	93.0%
Bulging size, mm	80.0%
Canal Diameter mm	80.0%
Foramen size mm	81.0%

Table 9

To prove workflow enhancement with a reduction of interpretation time of at least 20% (corresponding to a 1.25 ratio) that includes examination review and description of findings for herniation, stenosis, listhesis, L1S1 lordosis, and reduced disk height in lumbar spine MRI.

The average time for examination with and without the help of the software is filled in Table 11. The ratio of the average reading time with and without the assistance of the software will be shown to be not less than the ratio given in Table 10.

Average ratio of the time without the product and time with the product
1.25

Table 10

Average ratio of the time without the product and time with the product (95% CI)
1.48 (+/- 0.11)

Table 11

All results that are relevant to the claims are proven to be statistically significant by rejecting the relevant null hypothesis.

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