Summary of safety and clinical performance (SSCP)

ROTAIO

Cervical Disc Prosthesis

Manufacturer´s reference number: SSCP 002 ROTAIO

Created by:

Clinical Affairs Manager: ....
(Date) (Dr. rer. nat. Deepika Pothiraju)

Reviewed by:

Clinical Affairs Manager: ....
(Date) (Dr. rer. nat. Stefan Schumacher)

Reviewed and approved by:

Person responsible for
regulatory compliance
and managing director: ....
(Date) (Mareike Siedler)

Table of contents

Purpose

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the ROTAIO Cervical Disc Prosthesis by SIGNUS Medizintechnik GmbH.

The SSCP is not intended to

- give general advice on the diagnosis or treatment of particular medical conditions, nor
- replace the instructions for use (IFU) as the main document that will be provided to ensure the safe use of a particular device, nor
- replace the mandatory information on implant cards or in any other mandatory documents.

This SSCP contains information for users/healthcare professionals and patients. Therefore, the SSCP has four parts:

1. General Information for Users/Healthcare Professionals and Patients
2. Summary of Safety and performance data for Users/Healthcare Professionals
3. Summary of Safety and performance data for Patients
4. References

Change history

Version	Author	Date	History Description	Revision validated by the Notified Body
0	Dr. Stefan Schumacher	28.06.2022	First version	☐ Yes Validation language: English ☒ No
1	Dr. Stefan Schumacher, PD Dr. Ulrich Matern	30.03.2023	Update according to deviation report from mdc	☐ Yes Validation language: English ☒ No
2	Dr. Stefan Schumacher, Meryem Yilmaz, PD Dr. Ulrich Matern	23.04.2024	Update according to deviation report from mdc	☐ Yes Validation language: English ☒ No
3	Dr. Fatemeh Shekoohishooli, Dr. Stefan Schumacher	05.09.2024	Update according to deviation report from mdc	☒ Yes Validation language: English ☐ No
4	Dr. rer. nat. Deepika Pothiraju	01.10.2025	Annual update, according to MDR 2017/745 and Australian Therapeutic Goods (Medical Devices) Regulations 2002, last compiled 14.10.2024.	☐ Yes Validation language: English ☒ No

Terms, definitions and abbreviations

Term	Definition
ACDF	'ACDF' is the short form of Anterior Cervical Discectomy and Fusion. In ACDF, the intervertebral disc is removed and the adjacent vertebrae are fused to ensure stability.
Adverse event	'adverse event' means any untoward medical occurrence, unintended disease or injury or any untoward clinical signs, including an abnormal laboratory finding, in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational device; [Regulation (EU) 2017/745; Article 2 Definitions]
ASD	Adjacent segment disease (ASD) is defined as degeneration that develops at mobile segments above or below a fused spinal segment and usually develops after spinal fusion or other back surgeries.
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte
Benchmark Device	A benchmark device is a similar product whose data is used for comparison with the device to be evaluated.
Clinical data	clinical data' means information concerning safety or performance that is generated from the use of a device and is sourced from the following: - clinical investigation(s) of the device concerned, - clinical investigation(s) or other studies reported in scientific literature, of a device for which equivalence to the device in question can be demonstrated, - reports published in peer reviewed scientific literature on other clinical experience of either the device in question or a device for which equivalence to the device in question can be demonstrated, - clinically relevant information coming from post-market surveillance, in particular the post-market clinical follow-up; [Regulation (EU) 2017/745; Article 2 Definitions]
Clinical evidence	'clinical evidence' means clinical data and clinical evaluation results pertaining to a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer; [Regulation (EU) 2017/745; Article 2 Definitions]

Term	Definition
Clinical investigation	'clinical investigation' means any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device [Regulation (EU) 2017/745; Article 2 Definitions] Systematic investigation in one or more human subjects, undertaken to assess the safety or performance of a medical device. Note: 'clinical trial' or ' clinical study' are synonymous with ' clinical investigation'. [EN ISO 14155:2011]
Clinical performance	'clinical performance' means the ability of a device, resulting from any direct or indirect medical effects which stem from its technical or functional characteristics, including diagnostic characteristics, to achieve its intended purpose as claimed by the manufacturer, thereby leading to a clinical benefit for patients, when used as intended by the manufacturer; [Regulation (EU) 2017/745; Article 2 Definitions] Behavior of a medical device or response of the subject(s) to that medical device in relation to its intended use, when correctly applied to appropriate subject(s). [EN ISO 14155:2011]
FDA	The 'Food and Drug Administration' is the health authority responsible for U.S. market approval and monitoring of medical devices in the USA.
IDE	An 'Investigational Device Exemption' allows a medical device to be used in a clinical study conducted for market approval.
Incidence	The occurrence or frequency of an event within a specific population or group over a particular period.
Incident	'incident' means any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect; [Regulation (EU) 2017/745; Article 2 Definitions]

Term	Definition
Intended purpose	'intended purpose' means the use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use or in promotional or sales materials or statements and as specified by the manufacturer in the clinical evaluation; [Regulation (EU) 2017/745; Article 2 Definitions]
Instruction for use (IFU)	'instructions for use' means the information provided by the manufacturer to inform the user of a device's intended purpose and proper use and of any precautions to be taken; [Regulation (EU) 2017/745; Article 2 Definitions]
MDCG	Medical Device Coordination Group
MDR	Medical device regulation
Myelopathy	Myelopathy is caused by degeneration of the intervertebral disc and/or vertebral bones, resulting in narrowing of the spinal canal (spinal stenosis) ultimately causing compression of the spinal cord. Myelopathy can result in pain, weakness, altered sensation or difficulty controlling specific muscles.
Ossification	The process by which soft tissues in the body, like muscles or tendons, turn into bone.
Performance	'performance' means the ability of a device to achieve its intended purpose as stated by the manufacturer; [Regulation (EU) 2017/745; Article 2 Definitions]
Post-market surveillance (PMCF)	'post-market surveillance' means all activities carried out by manufacturers in cooperation with other economic operators to institute and keep up to date a systematic procedure to proactively collect and review experience gained from devices they place on the market, make available on the market or put into service for the purpose of identifying any need to immediately apply any necessary corrective or preventive actions;
PMCF study	A study carried out following the CE marking of a device and intended to answer specific questions relating to clinical safety or performance (i.e. residual risks) of a device when used in accordance with its approved labelling. [MEDDEV 2.12/2 rev.2]

Term	Definition
Radiculopathy	Radiculopathy, also commonly referred to as pinched nerve, refers to a set of conditions in which one or more nerves are affected and do not work properly. Pinched nerves arise when surrounding bone or tissue, such as cartilage, muscles or tendons, put pressure on the nerve and disrupt its function. Radiculopathy can result in pain, weakness, altered sensation or difficulty controlling specific muscles.
Risk	'risk' means the combination of the probability of occurrence of harm and the severity of that harm; [Regulation (EU) 2017/745; Article 2 Definitions] Combination of the probability of occurrence of harm and the severity of that harm. [EN ISO 14971:2012]
Risk management	Systematic application of management policies, procedures and practices to the tasks of analyzing, evaluating, controlling and monitoring risk. [EN ISO 14971: 2012]
UDI	Unique Device Identification

1 General Information for Users / Healthcare Professionals and Patients

The first chapter of this part contains regulatory information about the device, the manufacturer and the notified body. The second chapter provides information about the intended use as well as indications and contraindications. The device and its application are described in the third sub-chapter.

1.1 Device identification and general regulatory information

Aspect	Description
Device trade name:	ROTAIO Cervical Disc Prosthesis
Manufacturer's name:	SIGNUS Medizintechnik GmbH Industriestr. 2 63755 Alzenau
Manufacturer's single registration number (SRN)	DE-MF-000006200
Basic UDI-DI	ROTAIO Cervical Disc Prosthesis: 404784401020207052125
Medical device nomenclature description / text (EMDN codes)	L09070201
Class of Device:	Class III according to Annex VIII, rule 8 indent 9 (Regulation (EU) 2017/745)
Year when the first certificate (CE) was issued covering the device	2011
Authorized representative if applicable; name and the SRN	SIGNUS distributes and sales the device by itself
Notified body:	mdc medical device certification GmbH No. 0483

1.2 Intended use of the device

Aspect	Description
Intended purpose:	ROTAIO is a cervical disc replacement implant for use in the cervical spine. In addition to restoring height of the vertebral disc, its primary function is to preserve physiological mobility in the affected segment.
Indications	ROTAIO is indicated when the original intervertebral disc (C3 – C7) needs to be replaced due to radiculopathy and/or myelopathy and when the segment is still mobile. The patient's individual health condition must be taken into account by the treating surgeon.
Target population	No restriction of the skeletally mature patient population. The application of the devices is not limited to a certain patient profile (gender, age, weight etc.). However, the products are available in different sizes / diameters and are chosen by the responsible medical specialist in line with the individual anatomical situation of each single patient.
Contraindications and/or limitations	The ROTAIO Cervical Disc Prosthesis is contraindicated whenever primary stability of the device and mobility of the segment is not given due to pathological bone quality and anatomy, or when implants are contraindicated in general. The patient's individual health condition must be taken into account by the treating surgeon.

1.3 Device description

1.3.1 Function of the device

ROTAIO is a prosthesis to replace a defect intervertebral disc at the neck when non-surgical therapy failed, removal of the intervertebral disc with bony fusion is not desired, and ossification of the vertebral joints is not yet given.

The main function of ROTAIO, as with other prostheses, is to restore the distance between adjacent vertebrae so that the spinal nerves between them are not compressed. This main function - to act as a spacer between the vertebrae - can also be performed by so-called cages, which are small blocks, designed to create a bony fusion between the adjacent vertebrae.

In contrast to cages, ROTAIO and other prostheses enable further movements between the adjacent vertebrae. Unlike a door hinge, the movement between the vertebrae does not have a fixed rotational axis, but is more of a sliding movement. To mimic this movement, ROTAIO consists of parts that can slide freely to each other and can be angled and rotated at the normal degree of the spine.

Fig. 1: ROTAIO device in situ and technical drawings

To enable the normal movements of the spine and to restore the original height of the intervertebral space ROTAIO is designed as follows:

At the top and bottom, a metal (titanium) plate makes contact to the respective adjacent vertebrae. The plates are available in 4 sizes to fit to the size of the vertebrae (15x13, 17x13, 17x15, and 19x15 mm), and each size is available in 4 different heights (5, 6, 7, and 8mm) to fit the height of the intervertebral disc space. To select the correct size for an optimal fit, the surgeon must determine the size of the vertebral body surfaces intraoperatively using the accessory instruments. The bone-facing surfaces of the plates consist of multiple teeth that make immediate, rigid contact with the bone. For long-term stability, the surface is micro-roughened to allow bone ingrowth into the metal. This technique has been well established since the 1950s and is state of the art for almost all implants.

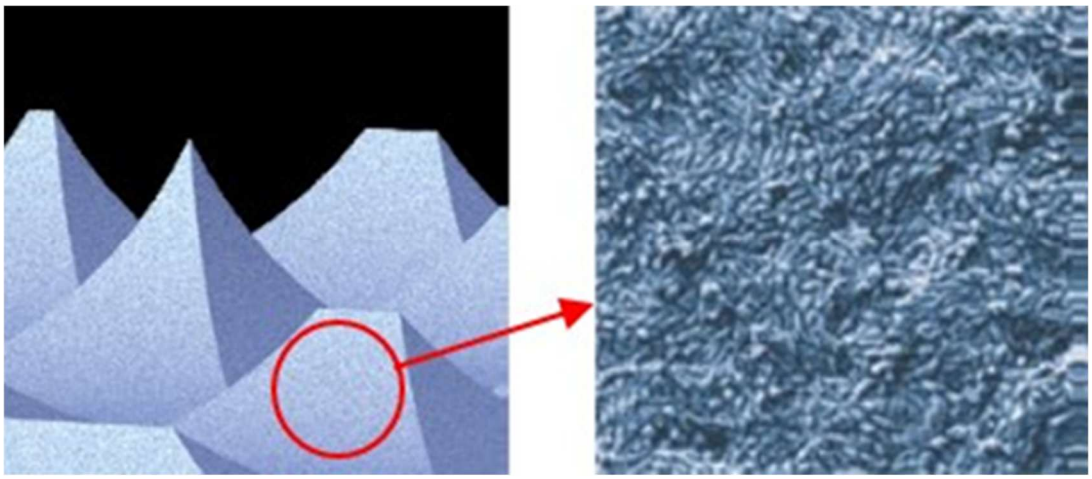

Fig. 2: The teeth of the titanium plate surface and a microscopic image after cell colonization

The titanium plates are fixed to the moving elements of the ROTAIO prosthesis. This moving mechanism consists of two metal sliding plates and a sliding disk in between that are connected by a keeper pin (all parts are made from CoCrMo). The patented mechanism allows free rotation (360°), flexion (16-20°) and sliding movements (2 mm) between the plates to maintain normal movement of the spine. The following figure demonstrates the sliding of the vertebrae above each other (yellow lines mark the adjacent vertebral bodies of the spine segment) and the respective motion of the ROTAIO device.

Due to its function of preserving mobility of the affected segment, ROTAIO is not intended to be combined with fixation such as plates or screws at the respective spinal segment.

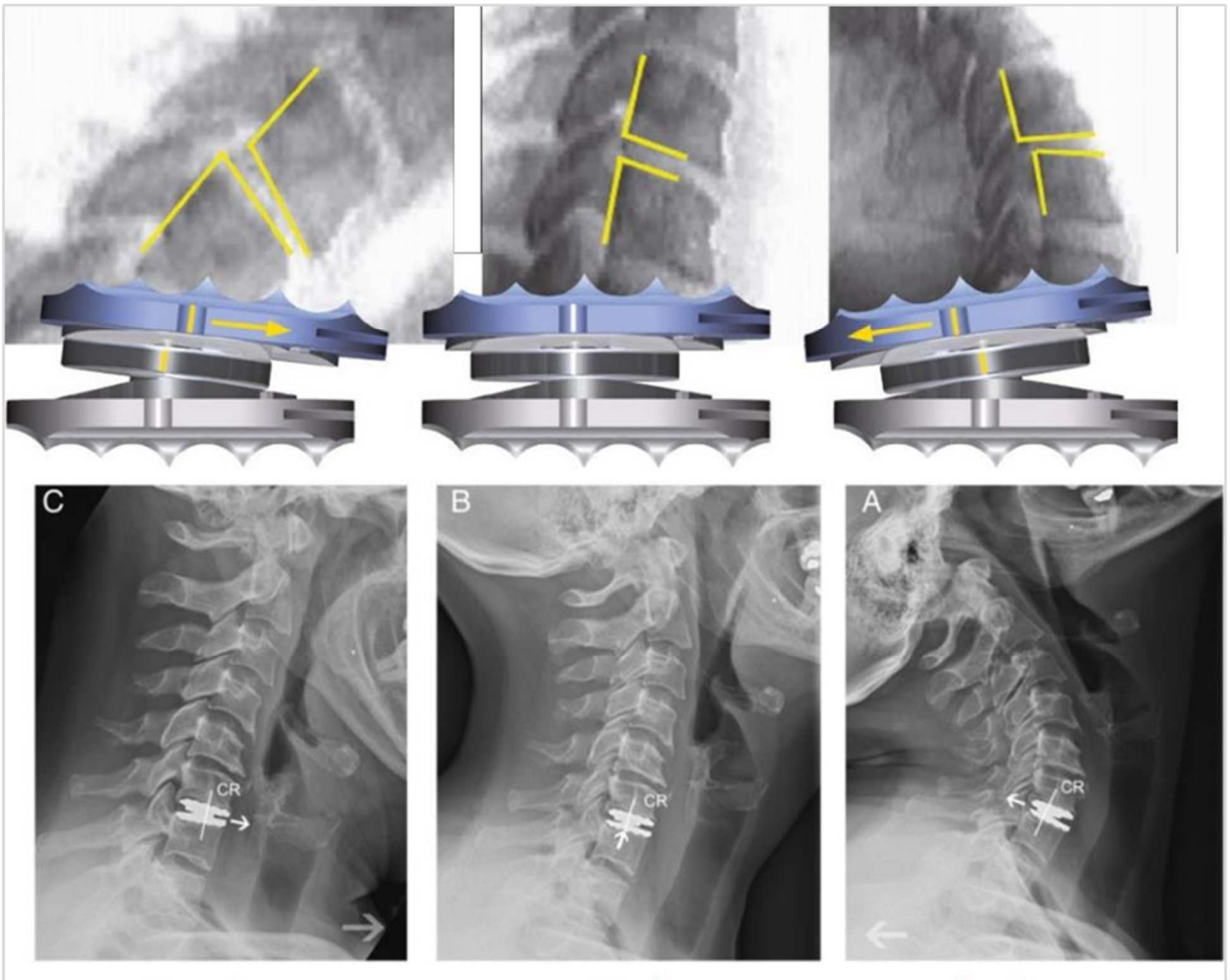

Fig. 3: Flexion (C), extension (A) and neutral position (B) of the spinal column with schematic and real translation and rotation of the device. CR = variable mechanical center of rotation.

1.3.2 Information about medicinal substances in the device, if any

ROTAIO does not contain any medicinal substances.

1.3.3 Implantation of the device

Similar to the removal of the intervertebral disc and spinal fusion with a cage implant, ROTAIO and other disc prostheses are implanted via an anterior approach. The surgical technique was first described in the 1950s and is still the gold standard to approach the intervertebral disc space at the neck. After frontal skin incision muscles, vessels, thyroid gland, trachea and esophagus are moved to the side to enable a small canal for the procedure at the intervertebral space. Then the disc is removed and replaced with the prosthesis, which is held in place by compression and teeth between the upper and lower vertebral bodies. A further fixation of the spine is not indicated to allow the desired mobility.

1.3.4 A reference to previous generation(s) or variants if such exist, and a description of the differences

Since the market launch of ROTAIO in 2011, the final product specifications of ROTAIO have neither been further developed nor changed in terms of product characteristics. No variants of ROTAIO other than the different product sizes are available.

1.3.5 Description of any accessories which are intended to be used in combination with the device

Instruments are available from SIGNUS for the discrimination of the correct size and the insertion and if necessary the removal procedure.

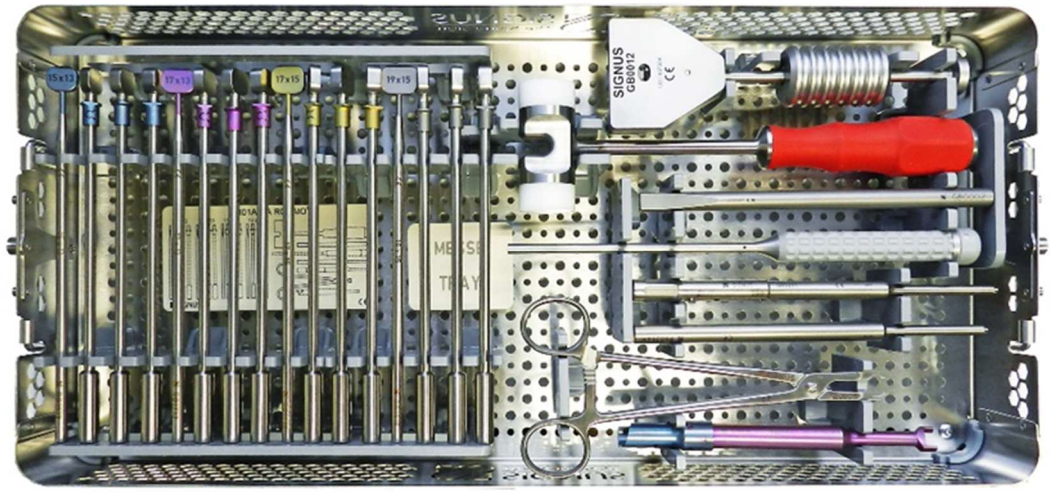

Fig. 4: Instrument tray

1.3.6 Description of any other devices and products which are intended to be used in combination with the device

There are no other devices and products which are intended to be used in combination with the device. Especially fixation of the respective spine segment with screws and plates is contradicted to maintain mobility.

1.4 Risks and warnings

1.4.1 Residual risks and undesirable effects

General risks associated with surgery or the complications that can arise from spinal surgery are not listed. The following are potential risks and complications which are related to the implant and which may necessitate repeat surgery:

- Loss of anchorage/fixation, subsidence or dislocation of the implant
- Sensitivity to foreign bodies, allergic reactions or other local / systemic adverse reactions to the implant materials used
- Incorrect placement
- Vascular lesion
- Neural lesions with reversible or permanent neurological deficits or paralysis
- Infection
- Wear, bending out of shape or breakage of implant components
- Temporary or permanent noise production
- Fusion of the segment that underwent surgery

These risks can potentially lead to injuries of all degrees of severity to the surrounding tissue, the nerves and blood vessels, which can in extreme cases even lead to death.

1.4.2 Warnings and precautions

1.4.2.1 Warnings

- The spinal implants and disposable instruments are intended for single use only and cannot be reused. Reuse may lead to failure of the implant or instrument, infection and/or death.
- SIGNUS implants may only be inserted with the instruments intended for this purpose. Correct implantation cannot be guaranteed if the implants are inserted using other instruments.
- The indication, selection and implantation are the responsibility of the using physician, who must be experienced and instructed in the performance of spinal interventions.
- Unless otherwise indicated, SIGNUS products must not be directly connected to the materials / components of other systems.

- Check the implant for scratches and other obvious damage. A damaged implant must not be used.
- When inserting the implant, particular attention must be paid to protecting the nervous structures and blood vessels, and increased force must be refrained from.
- Care must be taken to avoid over-distraction of the segment.
- Holding the dura away medially may cause additional damage to the spinal cord and possibly the nerves.
- An adapter is mounted on the sterile-packed ROTAIO disc prosthesis to facilitate insertion of the prosthesis into the intervertebral space. This adapter must be removed after implantation and must not remain in the patient's body.
- Postoperative care and follow-up examinations must be individually tailored to the patient and defined by the attending physician. After the procedure, physical activities of the patient should be allowed only to a very limited extent for an appropriate postoperative period. This applies in particular to lifting weights, twisting movements and any kind of sport. Falling or sudden jerky movements of the operated region should be avoided.

1.4.2.2 Precautions

- Keep sterile implants and instruments in their original packaging.
- Do not remove from the protective packaging until immediately before use.
- Before use, check the expiration date and the integrity of the sterile packaging. The product must not be used if the sterile packaging is damaged or the expiry date has been exceeded.
- Implants and disposable instruments are to be considered potentially infectious after use and are to be disposed of properly (special medical waste) in accordance with the applicable hygiene and waste disposal regulations. Instruments must be disposed of in the same way at the end of their life or reprocessed properly before disposal. Care must be taken to handle sharp-edged or pointed implants as well as instruments carefully to avoid injury.
- All information on the surgical technique, the implant assortment, the instruments and their use are described in detail in the SIGNUS product information. This information must be available on site and known to the surgical team.
- Before performing the operation, ensure that all necessary implants and instruments are available and in working order on site.
- The operation must be performed under fluoroscopy. The correct position of the implant shall be verified radiographically.
- The applied size indication is to be compared with that determined with the test specimen. Base area: Comparison of the base area information on the adapter with the information on the trial instrument used. Height: Observe the dot markings on the dorsal implant end plates (1 / 2 / 3 / 4 point(s) = 5 / 6 / 7 / 8 mm)

- Avoid excessive or complete ablation of the cortical base and cover plates.
- Carefully inspect disc cavity for bone particles after preparation.
- The implant must be firmly connected to the placement instrument intended for the implant to avoid damage to the implant and potential injury to the patient. Avoid injury to the patient.
- Do not impact the implant.
- Ensure that the implant has maximum contact with the adjacent vertebrae to avoid point loading.
- If it is necessary to remount the implant on the insertion adapter, this must be done according to the instructions in the sieve or in the product information.
- In case of repositioning of the prosthesis, it must be carefully grasped with the extraction forceps and pulled out. When doing so, increase the distraction in the affected segment and absolutely refrain from applying excessive force (e.g. by using the slotted hammer) in order not to damage the prosthesis. Before remounting on the insertion adapter, the integrity of the implant must be checked.
- In the postoperative phase, special attention must be paid to the individual information of the patient by the treating physician.

1.4.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN) if applicable

One Field Safety Notice (FSN) regarding a noise complaint was issued since the market launch and reported to BfArM. Additionally, the information about this noise complaint has been updated in the IFU and is considered one of the side effects of the ROTAIO application.

1.5 Suggested profile and training for users

Only surgeons experienced in spine surgery and orthopedic implants must use the ROTAIO system. SIGNUS offers teaching and training for surgeons and their teams at its webpage (www.SIGNUS.com).

2 Summary of Safety and Performance data for Users/Healthcare Professionals

The following text includes medical terminology that is not considered for patients. If you are a patient, please go to chapter 3.

2.1 Residual risks and undesirable effects

According to the analysis of the market feedback, clinical studies, and scientific literature, no systematic failures or complications related to ROTAIO were observed. Thus, the safety of ROTAIO is confirmed.

Nevertheless, as described in the instruction for use and chapter 1.4.1 of this SSCP residual risks from both the surgical procedure and the medical device remain.

The surgical approach to the spine, the removal of the original intervertebral disc and the insertion of the device was briefly described in chapter 1.3.3 of this SSCP. It is similar for mobile prostheses and cages for fusion. From the understanding of this surgical procedure, it is obvious that potential intraoperative complications are related to surgery and not the device itself. These device-unrelated complications are identical for solitary disc removal, fusion with a cage, or the insertion of a prosthesis like ROTAIO, and includes lesions of the organs, vessels and nerves next to the operating field, incorrect placement, and infection, as listed in chapter 1.4.1. These complications depend on factors that cannot be controlled by the manufacturer, but rather on situation-specific factors (e.g. surgical application, patient-specific factors).

In accordance with the "Summary of Safety and Clinical Performance MDCG 2019-9 v1 Quantitative data", we present the complications associated with clinical data that were proactively gathered through a structured prospective follow-up study of our device. A prospective multicenter trial of cervical arthroplasty with our medical device ROTAIO has demonstrated that there were no major complications. Temporary morbidity related to the anterior cervical approach but not the implant per se, like recurrent nerve palsy, significant dysphagia and myelopathy induced by posterior vertebral body osteolysis two years after undergoing CDA, occurred in 2 patients. Initially 6 patients experienced intermittent and transient cracking noises. Slight subsidence of the prosthesis was observed in 1 patient. Overall, total complication rate amounted to 9.2% and no procedures at the adjacent levels within last 3.5 years. [1].

Table 1: Complications (summarized based on sale volume 7952 since Jan. 2022 until 30.06.2025)

Complications	N (of cases)	%
Major complication	0	0
Transient approach related	2	0.025
Intermittent/transient cracking noises	6	0.075
Slight subsidence of prosthesis	1	0.0125
Fusion after 24 months	0	0
Revision at index level/foraminal stenosis	0	0
Operation at adjacent level (24 months)	0	0

Furthermore, another clinical and radiographic outcome analysis in a multicenter prospective trial with our medical device "ROTAIO"® Cervical Disc Prosthesis which was done in forty-one patients have shown that there were no signs of anterior migration or dislocation of the prosthesis. Subsidence was defined as a decrease of more than 2 mm in functional spinal unit (FSU) from 3 months to last follow-up and was observed in no patient. The sagittal alignment was well restored in all cases. Overall, the analyses of dynamic flexion and extension X-rays showed no malfunction of the prosthesis. Concerning the range of motion (ROM) a significantly increased motion was detected at every time point. The mean cervical spine motion in flexion-extension at the index level improved from 6.3° ± 2.9° preoperatively to 8.4° ± 2.5° at 3 to 6 months after surgery ($p < 0.001$) and to 8.6° ± 2.8° at last follow-up ($p < 0.001$). Radiographic analysis showed no dislocation, anterior migration or malfunction of the prosthesis. ROM values measured radiographically can be influenced by the radiographic technique itself, patient´s motivation or other – unknown – factors [4].

Moreover, wear, bending out of shape or breakage of implant components are further potential complications, but there was no report on any such events in a single scientific article about ROTAIO. Breakage and wear of benchmark devices were reported in the database of the American Food and Drug Administration (FDA) in 5 cases for a benchmark device. 2 cases of ROTAIO breakage complained to SIGNUS exclusively related to the removal of the devices for unknown medical reasons.

Temporary or permanent noise is a rare complication (0.14%) of the ROTAIO prosthesis that is not associated with limitation of motion. SIGNUS takes this very seriously and has conducted a series of internal and external tests and consulted medical experts to analyze this issue. CT scans, mechanical, histological and spectral analyses did not explain these noises. This phenomenon is known from other cervical disc prostheses, too [3]. An additional review of literature on hip prostheses shows that squeaking, cracking and clicking of these devices is still a common phenomenon occurring in 2-30% of cases even within the 4th generation of these implants [13].

Typical late complications of cervical prostheses are due to the pre-damaged spine and the progressive underlying disease. Preserving mobility with prostheses such as ROTAIO reduces the risk of heterotopic ossification and fusion of the segment, which was shown in several studies comparing fusion with prosthesis implantation, while other studies did not observe differences. The same is given for arm and neck pain and quality of live scores. [12]

From another side, biocompatibility was successfully tested in the pre-clinical phase, and neither in scientific literature nor in databases of health authorities there were hints that the materials used led to any undesired body reactions such as allergies or local reactions. However, theoretically the occurrence of such adverse reactions is possible.

SIGNUS tested the mechanical stability, biocompatibility, and sterility of the subject device extensively in the laboratory. Clinical studies and experience from market surveillance since the market launch in 2011 support safety and effectiveness of the device.

SIGNUS conducts continuous market monitoring in order to identify risks and to react immediately if necessary. Consequences of this effort are described in chapter 3.1.2. Furthermore, information material and training for surgeons, as well as patients following the instructions of their surgeons also reduces risks.

NOTE: It is the user's responsibility to ensure that the surgical procedure is performed correctly. Appropriate clinical training as well as a theoretical and practical proficiency of all the required operating techniques, including the use of this product, are prerequisites for the successful use of this product. SIGNUS offers teaching and training for clinicians and their teams at its webpage (www.SIGNUS.com).

NOTE: SIGNUS is not responsible for complications caused by failure to follow the warnings and precautions listed in chapter 1.4.2.

NOTE: The user is obligated to report all severe events in connection with the product to the manufacturer and the responsible authorities of the state in which the user is located.

2.2 Summary of clinical evaluation and post-market clinical follow-up (PMCF)

2.2.1 Summary of clinical data related to equivalent device, if applicable

Not applicable

2.2.2 Summary of clinical data from conducted investigations of the device after the CE-marking

2.2.2.1 Studies initiated by SIGNUS

Planned studies

SIGNUS submitted a study protocol application to the ethics committee for conducting a prospective PMCF study at University Hospital Innsbruck and is waiting for a registration number. After obtaining the registration number, the study will be started in October 2025 and recruitment will end in October 2026. The aim of this PMCF study is to obtain clinical data regarding safety and performance of the ROTAIO. The follow-up period is 24 months. The PMCF study report will be generated based on the study results and an analysis will be provided to the Notified Body.

The study will be registered at the German Clinical Trials Register

Completed studies

SIGNUS initiated a prospective observational multicenter study led by the Dept. of Neurosurgery of the University of Innsbruck. Additional centers were the Neurosurgical Departments of the Hospitals in Munich Bogenhausen and the University of Greifswald, Erfurt and Bern.

120 patients (60% female, 40% male, mean age 42.3± 8.3 years) suffering from myelopathy (n=16) and radiculopathy (n=104) receiving ROTAIO were enrolled between 2014 and 2019 in the trial and followed for 24 months.

Radiological findings (height, range of motion (ROM), fusion, subsidence, migration, as well as radiographic success) and clinical findings (neck disability index (NDI), health related quality of live, neck and arm pain) as well as complications and removal were compared to benchmark data of prostheses tested in studies for FDA approval (IDE studies).

Study results had been published by Fleck et al in 2022.

Highly significant clinical improvements were observed according to NDI and VAS ($p<0.0001$ (arm); $p<0.001$ (neck); $p=0.002$ (head)) at all postoperative time points. Analgesic medication could be reduced after 3 months in 91.3%, after 12 months in 87.1% and after 24 months in 95.2% of patients. Doctor`s visits for cervical spine problems have been reduced in 93.8% after 24 months. Patient`s overall satisfaction was high after 3, 12 and 24 months with 83.5%, 78.4% and 79.1% of patients, while 4.1%, 6.8% and 7.0%, respectively were not satisfied. The composite success rate was 77.5% after 12 months and 76.9% after 24 months. There were no major complications in this series. Temporary morbidity related to the anterior cervical

approach but not the implant per se, like recurrent nerve palsy and significant dysphagia, occurred in 2 patients. Slight subsidence of the prosthesis was observed in 2 patients (2.2%) and 3 patients demonstrated fusion after 24 months. 2 patients developed symptomatic foraminal stenosis, so that implant removal and fusion was performed. Revision rate thus amounted to 1.7% at the index level and no procedures at the adjacent levels within 2 years. The authors conclude that ROTAIO is a safe and effective treatment option with good to excellent clinical results and very low secondary surgery rates. [1]

2.2.2.2 Other studies

Obernauer et al published the clinical outcome of 45 patients after arthroplasty using ROTAIO in a prospective multicenter study. Follow-up was 24 months at maximum. Clinical outcomes were assessed by Neck Disability Index (NDI), visual analogue scale (VAS) scores for neck and arm pain, patients´ overall satisfaction and the usage of analgesics. Additionally, radiographic information including ROM of the functional spinal unit and signs of adjacent segment disease were recorded.

NDI and VAS scores showed significant improvement 6 months after surgery and at last follow-up ($p < 0.001$). Concerning overall satisfaction 95.7% of the patients showed good to excellent results at the last visit and a significant reduction of analgesic usage was observed ($p < 0.001$). Radiographic measurements showed a mean increase of ROM up to 8.40° in the treated segment at last follow-up ($p < 0.001$). No signs of anterior migration or dislocation of the prosthesis and no subsidence was recorded radiographically. Self-limiting dysphagia was detected in three patients, which was probably due to traction or laryngeal nerve irritation during surgery.

In other studies, adjacent segment disease (ASD) following uninstrumented ACDF has been reported to occur in 25 % of patients within 10 years and shows an incidence of 2.9 % per year. In the present study, radiographic ASD was defined as new anterior osteophyte formation or enlargement of existing osteophytes and the rate of reoperation at the level directly adjacent to the treated level. In one case (2.2 %) anterior bridging bone at the index level and new osteophyte formations in the adjacent cranial level were observed. Concerning the development of symptomatic ASD the results of this study show a mild increase in the mean VAS regarding neck pain from the 6 months visit to the last follow up. It remains unclear, if this is a result of the prosthesis or degenerative spine disease.

There were no other minor or major complications and no implant-related complications such as subsidence or fractured vertebrae. In one patient's revision, surgery at the index level was required (2.2 %). Caused by implantation of an undersized and too ventrally positioned prosthesis the patient suffered from increasing neck pain. A few weeks after the 12 months follow-up the prosthesis was removed, and the patient was treated with ACDF.

In the 24-month follow-up, ROTAIO provided excellent clinical and radiographical results and seems to be safe and effective for the treatment of symptomatic single-level degenerative disc disease. [4]

Landscheidt et al randomly reexamined 18 patients with single-level ROTAIO arthroplasty from the above study at 60 months follow-up and presented a poster at the 14th German Spine Congress 2019. Mean follow-up was 5.4 years. VAS scores for neck and arm pain were significantly reduced from 5.1±2.9 to 2.6±3.1 (p=0.023) and from 4.9±3.6 to 1.9±3.1 (p=0.004) respectively. The NDI was reduced from 18.2±10.9 to 11.3±11.6 (p=0.083). No significant differences were observed between 3, 6 months and 5 year data. Regarding patient satisfaction, 13 (72%) had met their expectations, 3 (17%) had not the expected improvement but would have the same surgery again and one patient (5.5%) was not satisfied. The authors rate ROTAIO as effective. [5]

Lang et al reported on 53 ROTAIO patients after one year follow-up. Pre- and postoperative ROM showed no significant changes (8.0° vs. 10.9°; p>0.05). Significant correlations between center of rotation and implant position (p<0.01) as well as between ROM and implant position (p=0.04) were revealed. NDI and VAS improved significantly from pre- to postoperative evaluation (p <0.01). No implant-related complications occurred, and no revisions were performed. Implantation of the ROTAIO prosthesis, which allows uncoupled translation, maintains ROM and results in a physiological center of rotation. The exact position of the device influences the clinical outcome. [6]

Elsawaf et al compared retrospectively the effect of the cervical fusion using a PEEK cage (ACDF) versus ROTAIO in 36 patients with a mean follow-up of 24 months ACDF was performed in 20 and an implantation of ROTAIO in 16 patients. NDI and the Japanese Orthopedic Association (JOA) score for myelopathy patients were used for preclinical and postoperative outcome measurements. In all patients, at final follow-up, a neuro-radiographic assessment was done. In the ACDF group the mean angle of the global cervical curve improved from 3.4° preoperative to 14.5° postoperative, whereas in the ROTAIO group the angle improved from 4.6° to 16.5° without statistically significant differences between both groups (p=0.6). The mean ROM at upper adjacent levels was 11.1°, and at the lower adjacent levels it was 10.2°. In the ROTAIO group the mean angle of ROM was 7.8° at upper adjacent levels and 9.6° at lower adjacent levels. Postoperative improvement of JOA and NDI scores was statistically significant (p<0.001) in the ACDF group, whereas in the ROTAIO group JOA improved from 15.7±1.2 to 16.2±1.1 and NDI improved from 19±2.1 to 16±8.7 without statistical significance. Symptomatic ASD was observed in 5 patients (20%) in the ACDF group and none in the ROTAIO group. Displacement of the prosthesis was shown in 2 patients, immediately after surgery. Both prostheses were removed immediately and placed again in a correct position. Otherwise, all other prosthesis showed a fair position. No other complications regarding the prosthesis itself were shown and no other complications with other cause are reported for both groups. The authors conclude: Compensatory increase in ROM of the adjacent segments in patients after ACDF may lead to ASD especially in those with asymptomatic adjacent sub-clinical degenerative disease. In contrast, arthroplasty reduces the incidence of adjacent segment diseases. [7]

Shin et al retrospectively studied radiological changes in adjacent and index levels after cervical disc arthroplasty in 125 patients with a mean follow-up of 38 months (range 25–114 months). Overall, 133 prostheses were implanted: 59 PRESTIGE, 26 ROTAIO, 15 Mobi-C, 13

ProDisc-C, 7 Activ C, 3 Discover, and 2 Baguera C. Radiographic data demonstrated mobility at both the index and adjacent levels, with no signs of hypermobility at an adjacent level. There was a non-significant loss of cervical global motion and range of motion of the functional spinal unit at the operated level, as well as the upper and lower adjacent disc levels, compared to the preoperative status. The cervical global and segmental angle significantly increased. Postoperative neck VAS, NDI, and JOA scores showed meaningful improvements after CDA. 29.6% of patients experienced heterotrophic ossifications. Four patients (3.2%) underwent reoperation due to failure of CDA. These patients received Mobi-C (2 cases), PRESTIGE (1 case), and Baguera C (1 case). The chief complaints of all patients requiring revision surgery were posterior neck pain and myelopathy with arm numbness and motor weakness. The causes of failure of the initial CDA were as follows: two patients had inadequate decompression and improper indications for surgery, including severe spondylosis or cervical instability; one had osteolysis and implant subsidence due to the selection of a too small prosthesis, and one resulted from inappropriate technique selection and instability. For resolution, two patients underwent two-level ACDF with a bone allograft and plate system, and the other two underwent laminectomy and lateral mass screw fixation. No device related complications occurred; all were related to the surgeon's indication, choice of implant and intraoperative technique. [8]

Jarmuzek studied the degenerative process after ACDF and CDA using the ProDiscC (2005-2011) and ROTAIO (since 2011) prostheses with a follow-up of at least 5 years. In total 63 patients were included in the study: 23 ProDiscC, 5 ROTAIO and 35 ACDF. Significant differences were found for heterotopic osteophytes in the anterior upper region of the adjacent cranial segment and in the posterior caudal region of the adjacent lower segment. Additional significance was given for the ossification of the anterior longitudinal ligament in favor of the treatment with a prosthesis. After 5 years, there were no significant differences in the disc height of adjacent segments or clinical symptoms between both groups. The prosthetic group also tends to calcify the treated segment over time. An evaluation between ROTAIO and ProDiscC was not performed. [9]

A recent study conducted by Anna Lang's group assessed the radiological and clinical correlation between the instantaneous center of rotation (iCOR) and range of motion (ROM) following cervical total disc replacement (cTDR). The iCOR of a motion segment has been shown to correlate with its total ROM. Notably, prior research has identified that the correct placement of cervical total disc replacements is crucial for preserving a physiological iCOR. This study analyzed changes in these parameters and their corresponding clinical relevance. In this retrospective multi-center observational study, researchers evaluated radiological and clinical parameters both preoperatively and one year after cTDR with an unconstrained device. Radiographic parameters, including flexion/extension X-rays (flex/ex), ROM, iCOR, and implant position in the anterior-posterior direction (IP ap), were assessed alongside clinical parameters such as the Neck Disability Index (NDI) and the visual analogue scale (VAS). The study analyzed 57 segments from 53 patients treated with cTDR. The pre- and post-operative ROM did not show significant changes (8.0° vs. 10.9°; $p > 0.05$). However, significant correlations were found between iCOR and IP ap (Pearson's R: 0.6; $p < 0.01$) as well as between ROM and IP ap (Pearson's R: −0.3; $p = 0.04$). Both NDI and VAS scores

improved significantly ($p < 0.01$). Additionally, a significant correlation between NDI and IP ap was found after 12 months (Pearson's R: −0.39; $p < 0.01$).

The implantation of the tested prosthesis maintains ROM and results in a physiological iCOR. The precise positioning of the device correlates with clinical outcomes, highlighting the importance of implant design and accurate placement. [16]

A recent study by Man Kyu Choi focused on myelopathy caused by posterior vertebral body osteolysis occurring two years after cervical disc arthroplasty (CDA). CDA has become increasingly popular and differs from the conventional technique used in anterior cervical fusion for treating cervical degenerative disc disease. Although arthroplasty is a favored treatment option, there have been few reports of complications in literature. These complications include subsidence, expulsion, posterior avulsion fractures, heterotopic ossification, and osteolysis. One critical complication is osteolysis, but current studies are limited in their examination of its incidence, etiology, and consequences. The authors present two cases of patients who exhibited clinical signs of progressively worsening myelopathy induced by posterior vertebral body osteolysis two years after undergoing CDA. Both patients subsequently underwent posterior decompression and fusion without the removal of the prosthesis. Postoperatively, their clinical symptoms gradually improved, and no severe deficits were noted. These rare cases emphasize the potential for osteolysis to occur after CDA, which can lead to cervical myelopathy, and highlight the need for spine surgeons to remain vigilant regarding this serious complication. [17]

Case study 1: Over a period of two years, the patient experienced complete relief from pain. However, they began to report a steady increase in axial neck pain and gait disturbances. To evaluate these new symptoms, a CT scan, MRI, and plain radiographs were obtained 25 months after the initial surgery. The imaging revealed lucency around the posterior margins of the endplates at the C4, C5, and C6 levels, along with myelopathy accompanied by signal changes. The radiographic study indicated severe osteolysis surrounding the artificial implant, extending to both the superior and inferior aspects of the endplates, as well as to the posterior wall of the vertebral body. This severe osteolysis raised concerns regarding the stability of the artificial implant and potential inflammatory complications, possibly including infection. Laboratory tests showed normal levels of C-reactive protein (<0.3 mg/dL), erythrocyte sedimentation rate (<10 mm/h), and white blood cell count (<8000 cells/mm³), without any signs of eosinophilia. As a result of these findings, prompt surgical intervention was performed, which included extended decompression and posterior fusion. Given the serious compressive lesions, a wide posterior decompression from C4 to C7 was carried out, along with posterior screw fixation extending from C4 to T1. Following the revision surgery, the patient reported improvements in neck pain and gait disturbances. At the 12-month follow-up, plain radiographs showed resolution of the osteolytic process and stable arthrodesis.

Case study 2: The patient initially maintained a fair condition, both clinically and radiologically, for approximately two years following the ROTAIO implant procedure. However, he subsequently experienced significant gait disturbances, unexpected sensations of electricity, and clumsiness during visits to outpatient clinics. To address his arm pain and myelopathic symptoms, a CT scan and MRI were performed 26 months post-surgery (see

below Figure). The results clearly indicated lucency around the posterior margin of the endplates at the C6 level and showed myelopathy with signal changes, consistent with the findings in case 1. Notably, there were no abnormal spinal movements or issues with the artificial implants, and laboratory tests revealed no increase in inflammatory markers. Given these complications, the patient required an additional intervention: a laminectomy and posterior fusion of the C5-6 vertebrae. Following this procedure, he was discharged a few days later, although he continued to experience numbness in both fingers.

➔ Osteolysis is a rare occurrence that can be observed even in high-end benchmark devices. According to existing literature, osteolysis that develops after one year may be associated with mechanical stress shielding and underlying vascular compromise. This emphasizes the importance of spine surgeons being vigilant about this serious complication.

2.2.3 Summary of clinical data from other sources, if applicable

Next to the abovementioned clinical studies after CE-marking and with regard to the safety and performance of ROTAIO, an expert report from the University of Innsbruck, Austria, reported in 2019 on experiences from 148 ROTAIO insertions between 2008 and March 2019:

"The surgical insertion of the prosthesis is facilitated by specific instruments, which allow implantation just like a cage. Thus, in comparison to cage fusion implantation of the prosthesis requires approximately 2 minutes extra, as positioning is done more precise and using continuous fluoroscopic control, which I don´t deem necessary for cage fusion. Implantation of the prosthesis is significantly faster (> 5-10 min) than anterior plating. The rectangular footprint of the prosthesis sits on the strong lateral bone of the vertebral endplates and covers a large area of the disc counteracting subsidence, which therefore has not been a concern in our experience with ROTAIO. The depth stop of the instruments avoids advancing the device into the spinal canal. [...] Insertion should be centered in the midline as much as possible, which is simplified by the large width of the device "forcing" the prosthesis centrally between the uncinated processes. This is supported by anteroposterior fluoroscopic control. As the device´s mechanism of motion allows mediolateral translation of up to 2 mm, this would even be correct for suboptimal midline positioning. Since the introduction of the prosthesis at the Department of Neurosurgery, no complaint needed to be made and transmitted to the manufacturer. Patients are routinely followed for 1 year according to an internal protocol of anterior cervical surgery. There were no device-related complications, but two cases were revised due to an unsatisfactory clinical result with chronic neck pain. As conservative management and cervical facet joint blocks did not clear the symptoms in these two patients, the prostheses were removed, and anterior cervical cage fusion (ACDF) was performed. A single patient demonstrated radiographic fusion at follow-up. Both revision rates and fusion rates compare favorably with the experience at our department with other cervical disc prostheses and with revision rates after ACDF.

Our results with the ROTAIO cervical disc prosthesis at the Department of Neurosurgery of the Medical University Innsbruck demonstrate that this prosthesis constitutes a safe and efficient treatment for its indicated use." [10]

2.2.4 An overall summary of the clinical performance and safety

The experiences made so far with ROTAIO and the benchmark have been presented and discussed in previous chapters.

These data demonstrate that ROTAIO performs well and safe and does not behave differently from the benchmark. Nevertheless, there are some residual risks of the procedure and the device that SIGNUS is aware of even when they were rarely or not described in the data sources reviewed. These residual risks are listed in chapter 1.4.1 of this SSCP document.

Cervical disc herniation has an estimated incidence of 5.5 per 100,000 people, with 26% of the cases being reported to require surgical interventions. Anterior cervical discectomy and fusion (ACDF) has been the most common procedure used for the surgical management of this disease. However, the limitations of ACDF have been well characterized. Most vexing has been the incidence of adjacent segment disease (ASD), which has been attributed to the acute alteration in motion segment mechanics. Therefore, alternative techniques were sought to address the problem, with the aim of preserving joint mobility. In the 1990s, artificial cervical discs emerged as an alternative to ACDF to preserve (as best) the physiological range of motion of the cervical spine. [11]

The mechanical properties of ROTAIO were tested in the laboratory and successfully compared with other state-of-the-art devices. ROTAIO has not broken in dynamic tests with 10 million cycles and a load corresponding to around 20 times the physiological load on the neck, which corresponds to a simulated service life of 80 years. This is also confirmed by the fact that SIGNUS has not received any information about broken devices under physiological stress since its market launch in 2011. Therefore, the implant is intended to remain in the body without defined termination, i.e. for the lifetime of the patient.

The clinical studies cited above demonstrate that ROTAIO produces results similar to benchmark devices, with no special complications outside the normal range of surgery.

According to the current knowledge based on the state of the art as well as the product-specific datasets provided by tests, clinical data and scientific literature, the benefits overweigh the risks of the application of ROTAIO. The analysis and assessment of potential risks has shown that there are no increased residual risks for patients, users or third parties in the context of the intended use of ROTAIO, which can be confirmed by the product-related clinical data. Risk reduction measures also were adequate.

The indications, contraindications and intended use defined for the ROTAIO are clear and cover an area that enables the user to achieve the expected goals.

The information materials provided by the manufacturer contain all relevant information to enable the user to a safe and reliable application of the ROTAIO within its intended use. With regard to the suitability of the intended population for the application of the device, this can be confirmed by the presented clinical data. The information presented in the IFU as well as in the various promotion materials are consistent and correct.

In conclusion, the presented and evaluated data confirms the safety and clinical performance of ROTAIO. The clinical studies cited above demonstrate that ROTAIO produces results

similar to benchmark devices, with no special complications outside the normal range of surgery. From a clinical point of view, the risk-to-benefit ratio is regarded as positive.

2.3 Ongoing or planned post-market clinical follow-up

In addition to the above-mentioned clinical data a further prospective observational study is planned, submitted to the ethics board and SIGNUS is waiting for registration number. Objective is the collection of long-term clinical data for a performance evaluation of associated with the ROTAIO implant in certified use. Primary endpoints are success rate, patient reported outcome measures, and safety as implied by revisions and the occurrence of implant- complications.

2.4 Possible therapeutic alternatives

In particular, a guideline recommends that after failed conservative therapy of intervertebral disc disease, surgical intervention is generally indicated to prevent the risk of destruction of the spinal cord and / or the spinal nerves with subsequent paralysis [15]. The surgical armamentarium includes several procedures including anterior cervical discectomy and fusion (ACDF) and cervical disc prostheses using devices such as ROTAIO. In contrast to ACDF devices, prostheses give the patient the chance of better mobility of the neck and less adjacent segment degeneration. In the review articles comparing ACDF and CDA, no distinction is made between the different devices from different manufacturers within the study subgroups. This supports the hypothesis that differences in performance and safety within both groups are very small and statistically or clinically irrelevant.

In contrast, meta-analyses demonstrate inferiority of ACDF especially for mobility of the neck (range of motion) and the development of adjacent segment disease (ASD). [11,12]

A prospective observational study with ROTAIO shows in comparison with clinical data of other prostheses that ROTAIO is not inferior to them; which is confirmed in scientific articles [1,4,5,6,7,11,12,14].

2.5 Suggested profile and training for users

See chapter 1.5.

2.6 Reference to any harmonized standards and common specifications (CS) applied

During the preparation of the report, the homepage of the EU Commission was searched for applicable Common Specifications. No applicable Common Specifications could be found which had to be taken into account in the preparation of this report.

The following table shows the harmonized standards which were applied to our product.

Table 2: Complications (summarized after 24 months in 92 patients)

Standard	Title	Edition
EN ISO 10993-1	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process	2020
EN ISO 10993-5	Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity	2009
EN ISO 10993-12	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials	2021
EN ISO 10993-18	Biological evaluation of medical devices - Part 18: Chemical characterization of medical device materials within a risk management process	2020
EN ISO 11137-1	Sterilization of health care products - Radiation - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices	2015/ A2:2019
EN ISO 11137-2	Sterilization of health care products - Radiation - Part 2: Establishing the sterilization dose	2015/A1:2023
EN ISO 11607-1	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems	2020/A1:2023
EN ISO 11607-2	Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes	2020/A1:2023
EN ISO 11737-1	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products	2018 / A1:2021
EN ISO 11737-2	Sterilization of health care products - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process	2020
EN ISO 13485	Medical devices - Quality management systems - Requirements for regulatory purposes	2016/AC:2018/A11:2021
EN ISO 14630	Non-active surgical implants - General requirements	2012
EN ISO 14971	Medical devices - Application of risk management to medical devices	2019/A11
EN ISO 15223-1	Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements	2021

3 Summary of Safety and Performance data for Patients

NOTE: The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an Implant Card or the Instructions for Use to provide information on the safe use of the device.

The general information about the device including product description and intended use are given in chapter 1.

The information presented in this chapter is intended for patients and laypersons.

3.1 Risks

NOTE: This document is not a substitute for consulting your doctor if you are concerned about side effects. The following points are an indication of when you should see your doctor. It may but does not have to be related to the device:

3.1.1 Remaining risks and undesirable effects

Contact your healthcare professional if you believe that you are experiencing one or more of the following symptoms. They may be related to the device or its use or a spinal disease.

Symptoms	Potential Cause
Fever Redness, swelling and pain at the wound	
New Neck or Arm Pain	New or increasing nerve irritation e.g. due to spine degeneration or ROTAIO issue
Weakness, altered sensation or difficulty degeneration or ROTAIO issue	

In the following, we explain these potential causes for the symptoms described in more detail and describe how frequently they have occurred with ROTAIO and comparable products.

The general risks associated with surgery such as vessel and organ injuries are assumed known and are therefore, not described here and need to be discussed with your surgeon.

Remaining risks from the medical device are:

- Foreign Body Reaction and Allergies are potentially given but not observed for ROTAIO so far.
- Loss of anchorage/fixation, subsidence or dislocation of the implant is a more realistic complication for cervical disc prostheses such as ROTAIO. According to the literature,

such events are observed in single studies with a probability of up to 6.5% for other prostheses, whereas for ROTAIO an occurrence rate of up to 3.3% is described. However, these numbers do not necessarily reflect the actual situation in clinical practice because they depend mainly on the surgical technique and bone quality of the individual patient. [1, 2]

- Wear, bending out of shape or breakage of implant components are further potential complications, but there was no report on any such events in a single scientific article about ROTAIO. Breakage and wear of benchmark devices were reported in 5 cases for a benchmark device to the American health authority. Two cases of ROTAIO breakage were exclusively related to the removal of the devices, which was performed for unknown medical reasons.
- Temporary or permanent noise production is a rare complication (0.14%) of the ROTAIO prosthesis. SIGNUS takes this issue very seriously and has conducted a series of internal and external tests and has engaged medical expertise to analyze this issue. CT scans, mechanical, histological and spectral analyses did not explain these noises. This phenomenon is known from other cervical disc prostheses, too [3]. The review of literature on hip prostheses shows that squeaking, cracking and clicking of these devices is still a common phenomenon occurring in 2-30% of cases even within the 4th generation [13].
- Preserving mobility with prostheses such as ROTAIO reduces the risk of segmental ossification, but there is no guarantee that the underlying disease will not progress and that mobility will be preserved forever [12].

3.1.2 How potential risks have been controlled or managed

SIGNUS tested the mechanical stability, biocompatibility, sterility of the subject device extensively in the laboratory. Clinical studies and experience from market surveillance since the market launch in 2011 support safety and effectiveness of the device. SIGNUS conducts continuous market monitoring in order to identify risks and react immediately if necessary. Consequences of this effort are described in chapter 3.1.2.

Furthermore, information material and training for surgeons, as well as patients following the instructions of their surgeons also reduces risks.

3.1.3 Summary of any field safety corrective action, (FSCA including FSN) if applicable

Since market launch in 2011, no risks or complications were identified that would have required action by SIGNUS. See chapter1.4.3.

3.2 Summary of clinical evaluation and post-market clinical follow-up

3.2.1 Clinical background of the device

Cervical disc herniation has an estimated occurrence of 5.5 per 100,000 people, with 26% of the cases being reported to require surgical interventions. Anterior cervical discectomy and fusion (ACDF) has been the most common procedure used for the surgical management of this disease. During this surgery, the pathologic intervertebral disc is removed and replaced by a block of bone or an artificial cage to maintain the space for the nerves.

However, the limitations of ACDF have been well characterized. Most vexing is the occurrence of adjacent segment disease (ASD), which is attributed to the acute loss of motion and the resulting overloading within the adjacent segments above and below the fusion.

Cervical disc herniation has an estimated occurrence of 5.5 per 100,000 people, with 26% of the cases being reported to require surgical interventions. Anterior cervical discectomy and fusion (ACDF) has been the most common procedure used for the surgical management of this disease. During this surgery, the pathologic intervertebral disc is removed and replaced by a block of bone or an artificial cage to maintain the space for the nerves.

However, the limitations of ACDF have been well characterized. Most vexing is the occurrence of adjacent segment disease (ASD), which is attributed to the acute loss of motion and the resulting overloading within the adjacent segments above and below the fusion.

3.2.2 The clinical evidence for the CE marking

ROTAIO was initially CE marketed in 2010 and launched to the market in 2011. Clinical evidence for CE marking is based on laboratory testing, scientific literature, market feedback, and clinical data with ROTAIO from clinical trials.

3.2.2.1 Clinical data from ROTAIO studies

SIGNUS completed a prospective observational multicenter study led by the Dept. of Neurosurgery of the University of Innsbruck. Additional centers were the Neurosurgical Departments of the Hospitals in Munich Bogenhausen and the University of Greifswald, Erfurt and Bern. 120 patients (60% female, 40% male, mean age 42.3± 8.3 years) suffering from myelopathy (n=16) and radiculopathy (n=104) receiving ROTAIO were enrolled between 2014 and 2019 in the trial and followed for 24 months. Radiological findings (height, range of motion (ROM), fusion, subsidence, migration, as well as radiographic success) and clinical findings (neck disability index (NDI), health related quality of live, neck and arm pain) as well as complications and removal were compared to benchmark data of prostheses tested in studies for FDA approval (IDE studies). Study results had been published by Fleck et al in 2022. The authors conclude that ROTAIO is a safe and effective treatment option with good to excellent clinical results and very low secondary surgery rates. More details can be found in reference [1].

Obernauer et al published the clinical outcome of 45 patients after arthroplasty using ROTAIO in a prospective multicenter study. Follow-up was 24 months at maximum. Clinical

outcomes were assessed by Neck Disability Index (NDI), visual analogue scale (VAS) scores for neck and arm pain, patients´ overall satisfaction and the usage of analgesics. Additionally, radiographic information including ROM of the functional spinal unit and signs of adjacent segment disease were recorded. In the 24-months follow-up, ROTAIO provided excellent clinical and radiographical results and seems to be safe and effective for the treatment of symptomatic single-level degenerative disc disease. [4]

Landscheidt et al randomly reexamined 18 patients with single-level ROTAIO arthroplasty from the above study at 60 months follow-up and presented a poster at the 14th German Spine Congress 2019. Mean follow-up was 5.4 years. VAS scores for neck and arm pain were significantly reduced from 5.1±2.9 to 2.6±3.1 (p=0.023) and from 4.9±3.6 to 1.9±3.1 (p=0.004) respectively. The NDI was reduced from 18.2±10.9 to 11.3±11.6 (p=0.083). No significant differences were observed between 3, 6 months and 5 year data. Regarding patient satisfaction, 13 (72%) had met their expectations, 3 (17%) had not the expected improvement but would have the same surgery again, and one patient (5.5%) was not satisfied. The authors rate ROTAIO as effective. [5]

Lang et al reported on 53 ROTAIO patients after one year follow-up. Pre- and postoperative ROM showed no significant changes (8.0° vs. 10.9°; p>0.05). Significant correlations between center of rotation and implant position (p<0.01) as well as between ROM and implant position (p=0.04) were revealed. NDI and VAS improved significantly from pre- to postoperative evaluation (p <0.01). No implant related complications occurred and no revisions were performed. Implantation of the ROTAIO prosthesis, which allows uncoupled translation, maintains ROM and results in a physiological center of rotation. The exact position of the device influences the clinical outcome. [6]

Elsawaf et al compared retrospectively the effect of the cervical fusion using a PEEK cage (ACDF) versus ROTAIO in 36 patients with a mean follow-up of 24 months ACDF was performed in 20 and an implantation of ROTAIO in 16 patients. NDI and the Japanese Orthopedic Association (JOA) score for myelopathy patients were used for preclinical and postoperative outcome measurements. In all patients, at final follow-up, a neuro-radiographic assessment was done. Compensatory increase in ROM of the contiguous adjacent segments in patients subjected to ACDF may lead to ASD especially in those with asymptomatic adjacent sub-clinical degenerative disease. In contrary, arthroplasty reduce the incidence of adjacent segment diseases. [7]

Shin et al retrospectively studied radiological changes in adjacent and index levels after cervical disc arthroplasty in 125 patients with a mean follow-up of 38 months (range 25–114 months). Overall 133 prostheses were implanted: 59 PRESTIGE, 26 ROTAIO, 15 Mobi-C, 13 ProDisc-C, 7 Activ C, 3 Discover, and 2 Baguera C. Radiographic data demonstrated mobility at both the index and adjacent levels, with no signs of hypermobility at an adjacent level. There was a non-significant loss of cervical global motion and range of motion of the functional spinal unit at the operated level, as well as the upper and lower adjacent disc levels, compared to the preoperative status. The cervical global and segmental angle significantly increased. Postoperative neck VAS, NDI, and JOA scores showed meaningful improvements after CDA. 29.6% of patients experienced heterotrophic ossifications. Four

patients underwent reoperation due to failure of CDA (with competitor prosthesis). No device related complications occurred; all were related to the surgeon's indication, choice of implant and intraoperative technique. The authors rate CDA as an effective surgical technique for optimizing clinical outcomes and radiological results. In particular, the preservation of cervical ROM with an artificial prosthesis at adjacent and index levels and improvement in cervical global alignment could reduce revision rates due to adjacent segment degeneration. [8]

Jarmuzek studied the degenerative process after ACDF and CDA using the ProDiscC (2005-2011) and ROTAIO (since 2011) prostheses with a follow-up of at least 5 years. In total 63 patients were included in the study: 23 ProDiscC, 5 ROTAIO and 35 ACDF. Significant differences were found for heterotopic osteophytes in the anterior upper region of the adjacent cranial segment and in the posterior caudal region of the adjacent lower segment. Additional significance was given for the ossification of the anterior longitudinal ligament in favor of the treatment with a prosthesis. After 5 years, there were no significant differences in the disc height of adjacent segments or clinical symptoms between both groups. The prosthetic group also tends to calcify the treated segment over time. An evaluation between ROTAIO and ProDiscC was not performed. [9]

3.2.2.2 Clinical data from other sources, e.g. market feedback

Next to the abovementioned clinical studies after CE-marking and with regard to the safety and performance of ROTAIO, an Expert-Report from the University of Innsbruck, Austria, reported in 2019 on experiences from 148 ROTAIO insertions between 2008 and March 2019. It says:

"The surgical insertion of the prosthesis is facilitated by specific instruments, which allow implantation just like a cage. Thus, in comparison to cage fusion implantation of the prosthesis requires approximately 2 minutes extra, as positioning is done more precise and using continuous fluoroscopic control, which I don´t deem necessary for cage fusion. Implantation of the prosthesis is significantly faster (> 5-10 min) than anterior plating. The rectangular footprint of the prosthesis sits on the strong lateral bone of the vertebral endplates and covers a large area of the disc counteracting subsidence, which therefore has not been a concern in our experience with ROTAIO. The depth stop of the instruments avoids advancing the device into the spinal canal. [...]. Since the introduction of the prosthesis at the Department of Neurosurgery, no complaint needed to be formulated and transmitted to the manufacturer. Patients are routinely followed for 1 year according to an internal protocol of anterior cervical surgery. There were no device-related complications, but two cases were revised due to an unsatisfactory clinical result with chronic neck pain. As conservative management and cervical facet joint blocks did not clear the symptoms in these two patients, the prostheses were removed and anterior cervical cage fusion (ACDF) was performed. A single patient demonstrated radiographic fusion at follow-up. Both revision rates and fusion rates compare favorably with the experience at our department with other cervical disc prostheses and with revision rates after ACDF. Our results with the ROTAIO cervical disc prosthesis at the Department of Neurosurgery of the Medical University Innsbruck

demonstrate that this prosthesis constitutes a safe and efficient treatment for its indicated use." [10]

In conclusion, the presented and evaluated data confirms the safety and clinical performance of ROTAIO. The clinical studies cited above demonstrate that ROTAIO produces results similar to benchmark devices, with no special complications outside the normal range of surgery. From a clinical point of view, the risk-to-benefit ratio is regarded as positive..

An overall summary of the clinical performance and safety going beyond the summary given here is presented in chapter 2.2.4.

3.2.3 Safety

The data of preclinical and clinical testing demonstrate that ROTAIO performs well and safe and does not behave differently from the benchmark. Nevertheless, there are some residual risks of the procedure and the device that SIGNUS is aware of even when they were rarely or not described in the data sources reviewed. These residual risks are listed in chapter 1.4.1 of this SSCP document.

The mechanical properties of ROTAIO were tested in the laboratory and successfully compared with other state of the art devices. ROTAIO has not broken in dynamic tests with 10 million cycles and a load corresponding to around 20 times the physiological load on the neck, which corresponds to a simulated service life of 80 years. This is also confirmed by the fact that SIGNUS has not received any information about broken devices under physiological stress since its market launch in 2011.

According to the current knowledge based on the state of the art as well as the product-specific datasets provided by tests, clinical data and scientific literature, the benefits overweigh the risks of the application of ROTAIO. The analysis and assessment of potential risks has shown that there are no increased residual risks for patients in the context of the intended use of ROTAIO, which can be confirmed by the product-related clinical data. Risk reduction measures also were adequate.

In conclusion, the presented and evaluated data confirms the safety and clinical performance of ROTAIO. Clinical data are similar to benchmark devices, with no special complications outside the normal range of surgery. From a clinical point of view, the risk-to-benefit ratio is regarded as positive.

3.3 Ongoing or planned post-market clinical follow-up

In addition to the above-mentioned clinical data, a further prospective observational study is planned, submitted to the ethics board and SIGNUS is waiting for registration number Objective is the collection of long-term clinical data for a performance evaluation of associated with the ROTAIO implant in certified use. Primary endpoints are success rate, patient reported outcome measures, and safety as implied by revisions and the occurrence of implant- complications.

3.4 Possible therapeutic alternatives

When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.

In general, when conservative treatment of disc disease fails, surgery is usually performed to prevent damage to the spinal cord or nerves, which can lead to paralysis.

A possible surgical alternative to the implantation of a mobile prosthesis such as ROTAIO, is fusion of the spine with a non-mobile device called a cage. In contrast to cages, prostheses offer the patient the opportunity for better neck mobility and, as a result, less degeneration of adjacent spinal segments.

3.5 Suggested training for users

See chapter 1.5.

4 References

1. Fleck S, Lang A, Lehmberg J, Landscheidt JF, Gerlach R, Rathert J, Ulrich C, Schär RT, Hartmann S, Mueller JU, Thome C. Prospective Multicenter Trial of Cervical Arthroplasty with the ROTAIO® Cervical Disc Prosthesis. Global Spine J. 2022 Aug 5:21925682221109563. PMID: 35929409

2. Burkus JK, Traynelis VC, Haid RW Jr, Mummaneni PV. Clinical and radiographic analysis of an artificial cervical disc: 7-year follow-up from the PRESTIGE prospective randomized controlled clinical trial: Clinical article. J Neurosurg Spine. 2014 Oct;21(4):516-28. PMID: 25036218

3. Siddiqui A, Wickham N, Hulme C. Painless squeaking following cervical disc replacement: A case report. Int J Spine Surg. 2015 Aug 12;9:44. PMID: 26484007

4. Obernauer J, Landscheidt J, Hartmann S, Schubert GA, Thomé C, Lumenta C. Cervical arthroplasty with ROTAIO® cervical disc prosthesis: first clinical and radiographic outcome analysis in a multicenter prospective trial. BMC Musculoskelet Disord. 2016 Jan 12;17:11. PMID: 26759165

5. Landscheidt J, Hartmann S, Thomé C.Reiser M, Lumenta CB, Lehmber J. Long-term patient-reported outcome after cervical disc arthroplasty. European spine Journal 2019;28:2736-2737

6. Lang A, Lener S, Grassner L, Abramovic A, Thomé C, Päsler D, Lehmberg J, Schär R, Hartmann S. Clinical and radiological outcome 1-year after cervical total disc replacement using the Signus ROTAIO - Prosthesis. Eur Spine J. 2022 Dec;31(12):3477-3483. PMID: 36219329

7. Elsawaf A, Faisal S, Hasanin M. Effect of Anterior Cervical Discectomy and Fusion Compared to Cervical Arthroplasty on Dynamics of Adjacent Segment Disease. Egy Spine J 2017;25:36-46

8. Shin JJ, Kim KR, Son DW, Shin DA, Yi S, Kim KN, Yoon DH, Ha Y. Radiological Changes in Adjacent and Index Levels after Cervical Disc Arthroplasty. Yonsei medical Journal 2022;63,1,72

9. Jarmuzek T. Evaluierung von Anschlussdegenerationen zervikaler Bandscheibenprothesenimplantation im Vergleich zur ventralen Platten-Schrauben-Spondylodese. 2017, Dissertation, Friedrich-Schiller-Universität Jena

10. Thomé C. ROTAIO cervical prosthesis – Surgeon's feedback: Clinical experience with the ROTAIO cervical prosthesis at the Department of Neurosurgery of the Medical University Innsbruck. 2019-03-08

11. Wahood W, Yolcu YU, Kerezoudis P, Goyal A, Alvi MA, Freedman BA, Bydon M. Artificial Discs in Cervical Disc Replacement: A Meta-Analysis for Comparison of Long-Term Outcomes. World Neurosurg. 2020 Feb;134:598-613.e5. PMID: 31627001

12. Gornet MF, Lanman TH, Burkus JK, Hodges SD, McConnell JR, Dryer RF, Copay AG, Nian H, Harrell FE Jr. Cervical disc arthroplasty with the PRESTIGE LP disc versus anterior cervical discectomy and fusion, at 2 levels: results of a prospective, multicenter randomized controlled clinical trial at 24 months. J Neurosurg Spine. 2017 Jun;26(6):653-667. PMID: 28304237

13. El-Desouky II, Helal AH, Mansour AMR. Ten-year survival of ceramic-on-ceramic total hip arthroplasty in patients younger than 60 years: a systematic review and meta-analysis. J Orthop Surg Res. 2021 Nov 18;16(1):679. PMID: 34794457

14. Summary of Safety and Effectiveness Data (SSED)
Prestige LP Cervical Disc
Medtronic Sofamor Danek
Date of FDA Notice of Approval: July 24, 2014
https://www.accessdata.fda.gov/cdrh_docs/pdf9/P090029B.pdf
download 2022-04-10

15. S2k-Leitlinie zur Versorgung bei Bandscheibenvorfällen mit radikulärer Symptomatik
AWMF-Registriernummer: 033-048 1
Version vom 28.06.2021
Leitlinie zur konservativen, operativen und rehabilitativen Versorgung bei Bandscheibenvorfällen mit radikulärer Symptomatik
https://www.awmf.org/uploads/tx_szleitlinien/033-048l_S2k_Konservativeoperative_rehabilitative-Versorgung-Bandscheibenvorfall-radikulae_2021-06.pdf
download 2022-04-09

16. Lang A(1), Lener S(2), Grassner L(2), Abramovic A(2), Thomé C(2), Päsler D(3), Lehmberg J(4), Schär R(5), Hartmann S(2). Clinical and radiological outcome 1-year after cervical total disc replacement using the Signus ROTAIO - Prosthesis. Eur Spine J. 2022 Dec;31(12):3477-3483. doi: 10.1007/s00586-022-07416-3. Epub 2022 Oct 11

17. J Korean Neurosurg Soc 66 (5) : 591-597, 2023
https://doi.org/10.3340/jkns.2022.0190 Cervical myelopathy induced by posterior vertebral body osteolysis after cervical disc arthroplasty. Man Kyu Choi, Jun Ho Lee