BRIEFING NOTE AND CONSENT FORM

«Study of the efficacy and tolerability of the B-Dyn medical device compared to a conventional bolted fusion, with or without cage, in the treatment of degenerative lumbar stenosis, with or without spondylolisthesis grade I, on the degree of a post-operative functional incapacity, of the preservation of mobility and the prevention of adjacent syndrome"

Interventional, prospective, comparative, randomized, non-inferiority, single-blind, international, multicentric clinical study.

BDYN STUDY- N° IDRCB: 2020-A00553-36

Mrs, Miss, Mr,

Dr _____(the investigator) practicing in/at_____ offers you the opportunity to participate in a research protocol. The proponent is the company: Biotech COUSIN, whose main office is located at the Allée des roses - 59117 WERVICQ-SUD – France. Before deciding whether or not you want to participate in this study, please take the time to read the following information carefully and to ask the investigating physician if you would like more information. If you decide to participate in this research, you will be asked for a written consent and you will then receive a copy of this document.

Your opposition to participate will not change in any ways your medical care, or your relationship with your doctor; likewise, you will fully have the right to withdraw your consent at any time without justification.

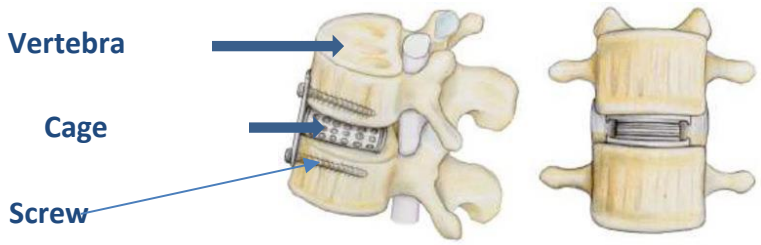
1. WHAT IS THE GOAL OF THIS RESEARCH?

You are being followed by the investigating physician for degenerative lumbar stenosis, with or without Grade I spondylolisthesis. This research focuses on the assessment of the effectiveness and safety of the B-Dyn device, in comparison to a conventional bolted fusion, with or without cage, for the treatment of degenerative lumbar stenosis symptoms.The B-Dyn device is already marketed in France and has already the CE marking.
To answer the research question, it is intended to include 216 individuals with degenerative lumbar stenosis, with or without Grade I spondylolisthesis, of which at least 100 participants in France.

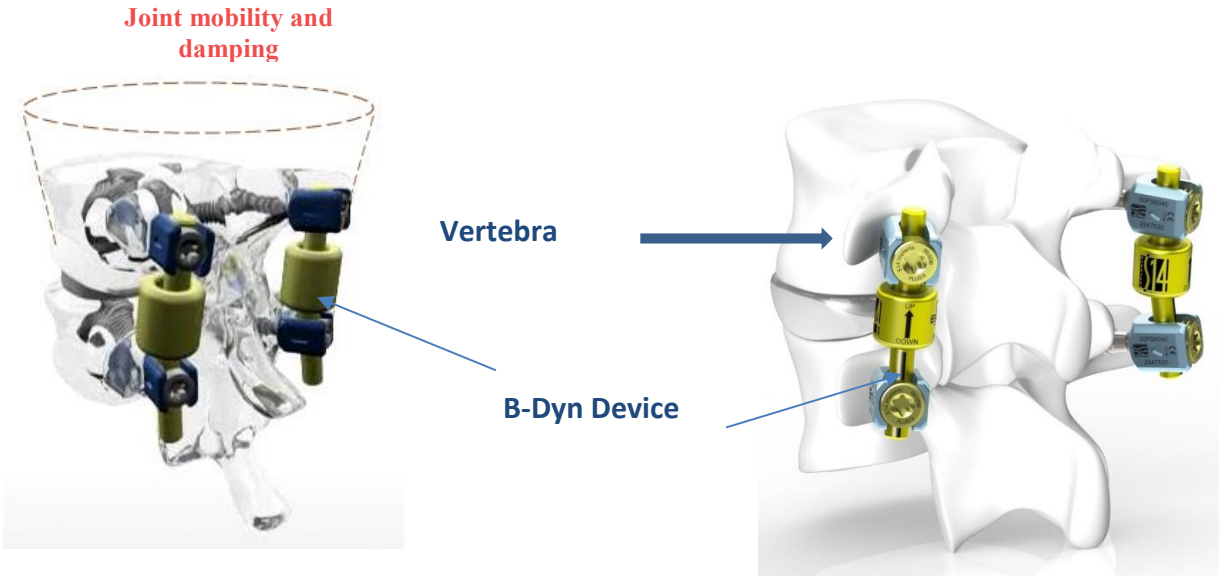
2. WHAT IS THIS RESEARCH ABOUT?

In the proposed research, we will assess the results of two surgical procedures: the implantation of the B-Dyn medical device, or a classical screwed l fusion with or without cage. In this research, you will benefit from one of the two interventions by random draw. You will then be under the care of the investigating physician as usual .
Degenerative lumbar stenosis is a narrowing of the spinal canal in the lower back. It causes pain and even disorders of the lower limbs, because the nerve roots are compressed. When a lumber vertebra slides forward and downward from the vertebra that is located just below, it drags the rest of the spine along with it; therefore, the term spondylolisthesis is used.

When the symptoms get worse and the individual feels functional discomfort, and pain becomes very disabling despite medical treatment, surgical intervention is recommended. Two surgical options are evaluated in this clinical research. The first one is screw fusion, with or without cage. Fusion, consists of «welding" two vertebrae together. To speed up the process and increase the success rate, implants (screws and cages) are used to immobilize the vertebrae. This is called rigid stabilization. These rigid stabilizations by screwed fusion with or without cages, constitute the current gold standard, i.e. the classically practiced procedure.



The second evaluated surgical option is the one conducted by the use of a dynamic stabilization system (B-Dyndevic) This system is called "dynamic" because it allows the stabilization of the operated part while preserving a certain mobility.



The B-Dyn device, manufactured by COUSIN Biotech (59117 Wervicq-sud – France), is a widely used device that preserves the mobility of the treated part. This device is implanted under general anesthesia.

How do these two interventions differ?

- By hypothesis, no difference is expected between these two interventions on the efficiency parameters such as pain, quality of life and functional capacities (walking, mobility).
- The loss of mobility caused by the fusion could be responsible several years later for the occurrence of damage to the joints above the operated level.
- However, using dynamic stabilization, partly preserving mobility, could prevent such degradation of the upper floors (this is one of the hypotheses that the study also seeks to demonstrate).

3. WHAT IS THE RESEARCH TIMELINE?

The duration of your participation in the study will be 5 years. If you decide to participate in this study, you will have to consult the investigating physician 5 times.
An **inclusion visit** will verify the inclusion and non-inclusion criteria. During this visit, a general clinical examination will be done by the investigating physician – this examination is being performed in a classical wayin the pre-surgical care of lumbar stenosis.

You will also perform: a preoperative lumbar spine MRI to confirm the existence of stenosis, an x-ray (Télé-rachis or EOS), a dynamic x-ray (in motion: flexion/extension and lateral inclination), and a test assessing your walking range (maximum walking distance). All these examinations are performed in a classical way, as in the pre surgical care of degenerative lumbar stenosis.

The following criteria are necessary for your inclusion in the study: you are 40 years old or older, registered in a social security scheme, you will be operated for the first time for a lumbar stenosis on 1 or 2 levels, with or without a grade 1 spondylolisthesis.

After signing your consent , you will also have to complete questionnaires in order to assess:

- The degree of your functional disability on a daily basis (Oswestry)
- The impact of lumbar stenosis on your quality of life (SF-12)
- The intensity of your lumbar pain and legs pain(Visual Analogue Scale(VAS))
- The impact of lumbar stenosis on your anxiety (Hospital Anxiety and Depression Scale)

Your neurological and motor status (assessed by the investigating physician, in your presence, on the MRC scale: Medical Research Council scale (which assess the motor function from 0: no movement/contractions to 5: normal muscle strength) and another scale from 0 (Absent) to 2 (Normal), to assess the sensation of touch and sting.

You will be hospitalized ,according to the centers' habits, where your surgeon practices, for less than 5 days or more if your condition requires it. During this hospitalization, several data will be measured to assess your potential post-operative pain, the time spent in the operating room and in the hospital, the amount of pain-killers consumed, or any side effects if there are.

Afterwards, **3 visits are planned: at 2 months, 12 months and 60 months after the operation**. During these visits, the investigating physician will conduct a clinical examination, he/she will have you complete the questionnaires listed above. You will perform an MRI (only at 12th and 60th months) and X-rays (tele-rachis and dynamic).

The visits will not exceed 1:30 hour each.

Any adverse events will also be recorded.

The consultations at 2 months and 12 months after surgery, are part of the usual follow-up care of degenerative lumbar stenosis surgery. The tests performed during these visits are the usual tests a patient undergo: radiography… etc. The Quality of Life, Neurological Status Assessment (MRC scale), and the anxiety self-assessments are added to the usual care that the patient receives. The MRI at 12 months is an additional test that is not part of the usual care at 12 months. The visit at 60months has been also added to the current practice.

4. WHAT ARE THE BENEFITS AND CONSTRAINTS OF YOUR PARTICIPATION?

Our hypothesis that the two evaluated surgical procedures (Fusion and B-Dyn stabilizing system) are equivalent and both allow reducing pain, improving quality of life and functional abilities as walking and mobility skills

Another hypothesis is that patients in the experimental group (BDYN) will maintain the upper level mobility and will have less adjacent syndrome in the long term compared to fusion patients.

If you agree to participate, you will have to respect the following points :

- Follow the medical instructions of the investigating physician and respect the scheduled visit dates. In the event that it is not feasible, please contact the investigating physician as soon as possible.
- Inform the investigating physician of the research, of any event occurring during the research period (hospitalization, etc.).
- Complete the questionnaires provided to you by the investigating physician.
- Be a beneficiary of a social security scheme
- Inform the investigating physician of any concomitant treatment prescribed by another physician or taken without a medical prescription.

Note that you will not be able to simultaneously participate in another research during your participation in this study; once you have signed your consent and until your participation is completed.

5. WHAT TREATMENTS ARE NOT ALLOWED DURING THE RESEARCH PERIOD?

No treatment is prohibited in this study.

6. WHAT ARE THE ANTICIPATED RISKS OF THIS RESEARCH?

Your participation in this research does not result in any additional risk compared to the risk incurred during surgery for the treatment of lumbar stenosis.

Complications are essentially those related to the surgical procedure:

- Complications of general anesthesia: these complications are detailed in the information sheet of the French Society of Anesthesia and Resuscitation, and are identical to those of any general anesthesia.
- The potential risks identified in the various available studies are the complications related to any spinal surgery. We will mention infections, bleeding, pain, leakage of cerebrospinal fluid, loss of neurological functions, etc. These complications will all be presented to you by your surgeon before the operation. The treatment of these complications is well known and the investigating physician knows how to deal with them.
- Other complications that may occur are related to the medical device itself.Loosening of one or all components
- Disassembly, bending and/or breakage of any or all of the components (screw breakage)
- The (allergic) reaction of foreign bodies to implants, debris, corrosion products ("fretting-corrosion" and/or general corrosion), including metallosis, tumour formation and/or the onset of autoimmune disease.
- Pressure on the patient's skin from implant components with inadequate tissue structure on the implant may cause skin penetration, irritation, fibrosis, neurosis and/or pain.
- Tissue damage or nerve disorders caused by incorrect positioning and placement of implants or instruments.
- Post-operative change in spinal curvature, loss of correction, height and/or reduction

These side effects are infrequent, their treatment is well known and the investigating physician knows how to manage them. It may be necessary to re-operate if any of these complications occur.

7. RESEARCH ORGANIZATION AND FUNDING

All the research costs will be covered by the proponent: COUSIN Biotech.

Costs related to the routine care such as the anesthesia consultation, cost excesses related to the surgery, all the tests and examinations falling within the framework of the usual care for the degenerative lumbar stenosis surgery, costs related to travel and accommodation are not covered by the proponent.

Costs associated with the 60-month visit (MRI, dynamic radiography, travel expenses) will be covered by the proponents of this research, this also applies to the 12-month MRI.

There is no allowance for participating in this research and no potential financial benefit can be derived from participating in the research, even if it leads to g marketed products.

8. WHAT ARE THE POTENTIAL MEDICAL ALTERNATIVES?

If you do not wish to participate in this study, your medical care will follow the usual protocol for treating degenerative lumbar stenosis.
The choice of surgical or medical alternative depends on the context (general condition, age, existence of diseases), on the experience of the investigating physician and on the patient's motivation.

9. WHAT ARE THE MODALITIES OF MEDICAL CARE AT THE END OF YOUR PARTICIPATION?

The investigating physician may decide at any time to end your participation and he will explain the reasons.
At the end of the research, or in the event of premature termination of the research, or premature termination of your participation, the investigating physician will decide on the frequency of visits thereafter.

- **At the end of the research, in the event that the research is terminated prematurely (by decision of the proponent or health authorities), if the research is excluded (by decision of the investigator) or if the study is discontinued (by decision of the individual):**

The medical care provided for you will not be changed. You will be checked upon at 2 months and 1 year post surgery. The 60^{th-}month visit will not be done (unless your doctor decides so).

10. IF YOU PARTICIPATE, WHAT WILL HAPPEN TO THE COLLECTED DATA FOR THE RESEARCH?

As part of the research in which COUSIN Biotech offers you to participate in, your personal data will be processed in order to analyze the results with regard to the objective of the study.

For this purpose, the medical data concerning you and the data relating to your lifestyle will be collected and transmitted to the company QUANTA MEDICAL, in charge of data processing, to the extent that these data are necessary for research.These data will be identified by a code number containing your inclusion order number, as well as the first letter of the surname and the first letter of the first name. These data may also be transmitted to the French Health Authorities under condition ensuring their confidentiality, . All data obtained during the study will be treated confidentially and securely.

For any cessation of participation without withdrawal of consent (premature cessation by decision of the proponent or health authorities), the data collected previously, before this cessation will be used. In the event that you no longer wish to participate in this research, and you wish to use your right to withdraw your consent, the use of your data collected on the basis of your consent before it is withdrawn, will be retained for research purposes.

11. HOW IS THIS RESEARCH FRAMED?

This research is carried out in accordance with Articles L1121-1 and following of the Public Health Code, relating to the protection of individuals who wilingly participate to researches involving the human person. This study is organised in accordance with the Helsinki Declaration, with the recommendations of the Good Clinical Practice and with thenational regulations. It has received the favourable opinion from the Committee for the Protection of Persons …….. as of ……

In accordance with the law, the proponent COUSIN Biotech, contracted an insurance policy N° 0100534514058 200031. guaranteeing its civil liability and that of any person working with **BIOMEDICINSURE**.

If you believe that you have suffered harm as a result of your participation in this research, you should immediately contact the investigating physician.

12. WHAT ARE YOUR RIGHTS ?

Your participation in this research is entirely free and voluntary. Your decision will not affect the quality of the care and treatment you should be expecting. Throughout the research, you will be able to ask the investigating physician for an explanation on the research process.

You may withdraw from the research at any time without justification, without any impact on your actual treatment, nor the quality of care provided to you and without any impact on your relationship with the investigating physician. After your withdrawal, you can still be under the care of the same medical team.

You may be accompanied by a trusted person of your choice during your visits.

In accordance with the provisions of the French «Informatique, Fichiers et Libertés » (law no. 78-17 as amended in 2004) and with the Law No. 2018-493 of June 20th 2018 on the protection of personal data transposing/adapting into French law, the General Regulation on the Protection of Personal Data (GRPD No. 679/2016), you can access the information on your medical file.

After consultation and agreement with your doctor, you will have the rectification right, the portability[1] right or the right to limit their use. You also have the right to object to the transmission of the data covered by the obligation of professional secrecy, which may be used and processed for this research. These rights are exercised by the investigating physician, who is the sole person that knows your identity.

You can also access all your medical data directly or through a doctor of your choice in accordance with the provisions of the article L 1111-7 of the Public Health Code.

Your medical file will remain confidential and may only be consulted under the responsibility of the investigating physician involved in your treatment, by the health authorities, and by the persons duly authorized by the proponent to participate in the research, noted that they are all subject to professional secrecy.

At the end of the research, and after analyzing the data relating to this research, you will be able to be informed of the overall results via the investigating physician working on this research.

The retention period of your personal data shall not exceed two years after the last publication of the research results or, in the absence of publication, they will be retained until the final research report is signed. Afterwards, they will be archived for 15 years.

[1]The right to portability offers the person/patient the possibility of retrieving part of his/her data in an open and readable format suitable for a device.The right to portability offers the possibility to recover the data, actively provided by the person/patient, for his personal use.

For research purposes, your personal data will be pseudonymized and transferred to a third country outside the EU for processing. In this regard, you have the right to obtain a copy of the reference to the appropriate guarantees.

With regard to any question concerning your personal data, you can – at any time - consult the Data Protection Officer of the Proponent at the following address (email address): B.Hill@quanta-medical.com . You are also informed that you can submit a complaint to the CNIL.

If you agree to participate in the research after reading all this information, and after discussing all the different aspects that are related to the research with the investigating physician, youmust sign and date the consent form at the end of this document.

If you have any questions about this study, feel free to ask the investigating physician:

Dr _____, telephone number: _____

Regardless of your decision regarding your participation, we thank you for your time and for your attention.

Confidential

Original : investigator
copy : patient

«Study of the efficacy and tolerability of the B-Dyn medical device compared to a conventional bolted fusion, with or without cage, in the treatment of degenerative lumbar stenosis, with or without spondylolisthesis grade I, on the degree of a post-operative functional incapacity, of the preservation of mobility and the prevention of adjacent syndrome"

Interventional, prospective, comparative, randomized, non-inferiority, single-blind, international, multicentric clinical study.

B-Dyn Study- N° IDRCB: 2020-A00553-36

Proponent : COUSIN Biotech, Allée des roses - 59117 WERVICQ-SUD – France

SECTION OF THE INVESTIGATOR : (to be completed by the investigator)

Investigator name : .....
Place : .....
Telephone number : .....
I confirm that I have provided detailed explanation regarding the clinical trial on the patient. I provided the patient with a briefing note and answered all of his/her questions about the study.

Date : ____/_____/_____ **Investigator signature :**
…….

SECTION FOR THE PATIENT : ***(To be completed by the patient)***

Patient name : .....
Patient first name : .....
Patient's mailing address: .....
.....
I have received and read the briefing note for the above study. I have also been informed of the purpose of this research, and its risks, by the investigating physician, of how it will be carried out and what my participation will involve me. I have received all the answers to the questions I asked him.
I have taken some time to think before taking this decision. I can ask the investigating physician for additional information at any time.

I know that it is my decision to take part in this study and that I have the right to change my mind at any time during the study without incurring any responsibility or prejudice in regards to the quality of care that will be provided to me in the future. I will then inform the investigating physician.

I have been informed that my participation in this research will last 60 months.

I know that all the data obtained during the study will be treated confidentially.

I agree that the data recorded in this study, containing personal data, may be processed electronically by or on behalf of the proponent.I consent that this data may be forwarded to health authorities.

I have received a copy of this document, which I will keep.

On this basis, I agree to participate in this study.

My signature does not discharge the investigator and the Proponent of all their responsibilities, and I retain all my rights as guaranteed by law.

Date : _____/_____/_____ Patient Signature:

……