The efficacy and safety of internal defibrillation: evaluation of the iD-System™, One-Handed Disposable Internal Defibrillation System

Protocol Version 1.0, 28 November 2017

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SUMMARY

Title	The efficacy and safety of internal defibrillation: evaluation of the iD-System™, One-Handed Disposable Internal Defibrillation System
Acronym	Internal defibrillation: iD-System™
Principal Investigator	Dr. Maud Beran
Version & date	Version 1.0, 28 November 2017
Company	SMART Clinical Products
Study site	Ziekenhuis Oost-Limburg
Study period	February 2018-April 2018
Rationale	The iD-System™ is designed for internal defibrillation in the same manner as the conventional internal paddles, which are used during intra-thoracic surgery. It delivers a shock to a patient's heart to restore normal sinus rhythm. The iD-System is a one-handed disposable medical device reducing the risk of cross contamination and the cost of sterilization. Moreover, it can be used in small-incision surgery due to its small size making it attractive for use in cardiac surgery.
Objectives	The main aim is to evaluate the safety and efficacy of the iD-System Safety: - To assess the ease of use of the device - To assess possible complications Efficacy: - To assess a successful restoration of the sinus rhythm
Investigational material and comparator products	The iD-System™ consist of two components: 1. The iD-Paddle™ is a disposable sterile one-handed paddle. The iD-Paddle is placed in contact with the heart when needed to deliver a shock to restore normal sinus rhythm. 2. The iD-Electrode™ is a disposable non-sterile electrode pad placed on the back of the patient and connected to the same defibrillator as the iD-Paddle. Both the iD-Paddle™ and the iD-Electrode™ are connected with the defibrillator/monitor via the iD-SMART Cable. The iD-SMART Cable ensures that the Internal Joules Protocol will be initiated, with a maximum of 50 Joules. The iD-SMART Cable is specific for each type of defibrillator/monitor.
Number of subjects planned	100 patients with cardiac surgery, approximately 10% with need of internal defibrillation
Duration of study	3 months

Inclusion and exclusion criteria	Inclusion criteria
	- All races and ethnicity (>18 years)
	- Written informed consent form (ICF) has to be obtained from the patient.
	- Elective surgery: cardiac surgery on pump (CPB)
	  o Coronary artery bypass surgery
	  o Heart valve repair and/or replacement
	  ▪ Mini sternotomy
	  ▪ Median sternotomy
	  o Redo surgery
	
	Exclusion criteria
	- Patients without cardiopulmonary bypass (referred to as heart-lung machine or pump)
	- Emergency surgery without a sufficient amount of time to explain and ask for ICF

Study design	Prospective interventional study with medical device

1. ETHICS

1.1. Independent Ethics Committee

The protocol and local Informed Consent Form must be reviewed and approved by the institution's Independent Ethics Committee (IEC) prior to the initiation of patient enrolment. The IEC will be notified of all subsequent protocol amendments. In addition, progress reports will be submitted to the IEC by the investigator as indicated by IEC's guidelines.

1.2. Ethical conduct of the study

The study will be conducted in accordance with the protocol, the principles that have their origins in the Declaration of Helsinki, as well as ICH GCP (Version 4, June 1996) and applicable national and local regulatory requirements, including but not limited to the Belgian Laws of 7 May 2004 relating to experiments on the human person (LEH), of 22 August 2002 on Patients' Rights and of 8 December 1992 (as amended) regarding the Protection of Privacy in relation to the Processing of Personal Data. All essential documents will be archived.

1.3. Patient information and informed consent

The informed consent will contain all elements required by ICH GCP. Written informed consent will be obtained from the patient prior to enrolment and participation of the study subject. The study centre further commits to conduct the study only on the basis of prior written consent by the subjects.

2. INVESTIGATORS AND STUDY ADMINISTRATION STRUCTURE

2.1. **Investigators**

Ziekenhuis Oost-Limburg will enroll approximately 100 patients. The trial will be supported by SMART Clinical Products by providing an internal defibrillation device and materials as specified above. SMART Clinical Products will be responsible for the technical support during the entire study period.

2.2. **Steering committee**

The Steering Committee will be responsible for the overall design, conduct, and supervision of the trial, including the development of the protocol and any protocol amendments. The Steering Committee meets periodically to assess the progress of the study to ensure subject safety and study integrity. The Steering Committee is composed of designated academic leaders and clinical experts.

Principal Investigator
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Co-investigators
Dr. Matteo Pettinari (MD)
Dr. Herbert Gutermann (MD)
Dr. Dieter Mesotten (MD PhD)

3. INTRODUCTION

In the majority of cardiac surgical interventions, cardiopulmonary bypass (CPB) is used because of the difficulty of operating on the beating heart. CPB is referred to as a heart- lung machine as the technique temporarily takes over the function of the heart (pump blood) and lungs (supply oxygen to red blood cells) during surgery (1). However, it is common for the post ischemic heart to fibrillate immediately after reperfusion and prior to weaning from extracorporeal circulation. This is referred to as ventricular fibrillation or tachycardia where cardiac electric shocks are often needed to restore the sinus rhythm of the heart (figure 1) (2,3). Therefore, intraoperative cardiac defibrillation is needed of which the most popular system consists of two spoon electrodes applied directly to the epicardium. The paddle handles are held by a surgeon when the electric current is passed from one spoon electrode through the patient's heart to a second spoon electrode (4). With the current tendency to reduce incision length in cardiac surgery, these paddles often turn out too bulky (5). Additionally, prior to use, the defibrillation handles and electrodes must be sterilized properly to eliminate patient infection. The handles have to be replaced after 25 cycles using steam sterilization or 100 cycles using hydrogen

peroxide gas sterilization (6). Independent of the sterilization, a defibrillation test has to be performed using a defibrillator analyzer after ten sterilization cycles or quarterly whichever comes first. The internal electrodes have to be replaced after 10 cycles using steam and 1 cycle using gas sterilization.

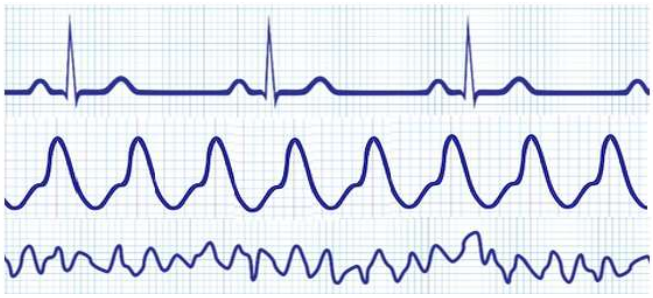

Figure 1: Normal and pathological electrocardiograms (ECG) related to internal fibrillation during cardiac surgery

Recently, with this knowledge, studies have shown that systems using a single paddle and an external adhesive pad positioned at the patient's back reached the same reliability and function (5).

SMART Clinical Products developed a disposable device (iD-System™, One-handed Disposable Internal Defibrillation System; figure 2) consisting of a single paddle (iD-Paddle) designed with a flexible head to maximize the contact with the heart. The adhesive pad (iD-Electrode), positioned at the patient's back, serves as a positive pole to guarantee an electric circuit transferred from a defibrillation device to the patient's heart. The iD-Sytem™ is connected to the defibrillator/monitor, via a specific iD-SMART Cable. More information about the product, the company and their strategy is provided in the evaluation plan (attachment 1) and the brochure (attachment 2).

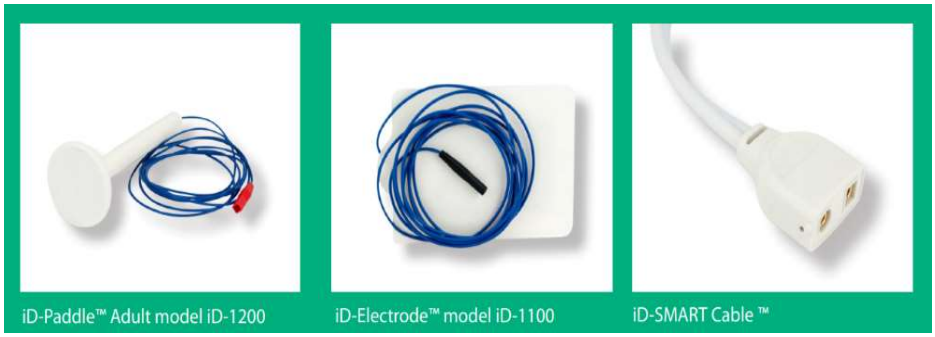

Figure 2: the iD-System™ developed by SMART Clinical Products consisting of the iD-Paddle, the iD-Electrode and the iD-SMART Cable.

In UZLeuven, this device was tested and the following conclusions were made in comparison to the conventional system (5)

- it can easily be used as a hybrid (both external and internal cardioversion) system
- it consists of disposable materials (reducing the risk of cross contamination and the cost of sterilization process). The iD-SMART Cable is a reusable product. The iD-SMART Cable will not be in direct contact with the patients tissue.

- its small size and single contact point approach permits safe use in limited access conditions such as with small-incision surgery and in redo surgery associated with extensive adhesions.

Since it is the current that defibrillates, impedance or resistance is important. With constant energy selected on the defibrillator device, defibrillation effectiveness is related to the resistance between the defibrillator and the patient's heart (7). The lower the resistance or impedance, the higher the defibrillation success. Myocardial injury associated with defibrillation corresponds not only with total joules used (energy), but also with the time interval between the defibrillation shocks. Therefore, throughout the cardiac surgery, perioperative myocardial damage is measured by electrocardiogram (ECG) and by cardiac troponin levels. Troponin levels indicate the severity of cardiac damage(8).

4. OBJECTIVES

The main aim is to evaluate the safety and efficacy of the iD-System™, One-handed Disposable Internal Defibrillation System The device is made for manual defibrillation during intra-thoracic procedure, by transferring a shock from a defibrillation device to the patient's heart, in combination with the iD-Electrode. The device will be used when the patient reaches a stage of ventricular fibrillation or rapid ventricular tachycardia during cardiac surgery.

- Safety:
    - To assess the ease of use of the device:
        - Adherence of the iD-Electrode to the patient's back
        - Positioning of the iD-Paddle for maximal contact with the heart
        - Working length of the following cables: iD-Electrode, iD-Paddle and the iD-SMART Cable
        - Applicability in small-incision surgery: mini sternotomy
    - To assess possible complications:
        - Skin symptoms to the electrode
        - Myocardial injury: troponin measurement

- Efficacy
    - To assess a successful restoration of the sinus rhythm
        - Number of failed attempts to defibrillate which were attributable to device malfunction.

5. INVESTIGATIONAL PLAN

5.1. **Patient population**

All patients undergoing cardiac surgery, meeting all inclusion and no exclusion criteria, are asked to participate.

5.2.1. Inclusion criteria

- All races and ethnicity (>18 years)
- Written informed consent form (ICF) has to be obtained from the patient.
- Elective surgery: cardiac surgery on pump (CPB)
    - Coronary artery bypass surgery
    - Heart valve repair and/or replacement
        - Mini sternotomy
        - Median sternotomy
    - Redo surgery

5.2.2. Exclusion criteria

- Patients <18 years
- Patients without cardiopulmonary bypass (referred to as heart-lung machine or pump)
- Emergency surgery without a sufficient amount of time to explain and ask for ICF

5.2. **Study design**

The iD-System™, One-handed Disposable Internal Defibrillation System is already tested by the biotechnical department of Ziekenhuis Oost Limburg (ZOL) which ensured proper working between the iD-System and the used defibrillator/monitor in ZOL (LIFEPAK® 20) (attachment 3 and attachment 3.1). In every included patient undergoing cardiac surgery on CPB/pump (during February 1st 2018 until April 30rd 2018), the iD-Electrode is placed prophylactically on the patient's back and is connected to the defibrillator in case ventricular fibrillation would occur. In every patient, the usability of the iD-System is determined according to a questionnaire focused on safety (figure 1: step 1-4, step 6). The questionnaire is available in attachment 4.

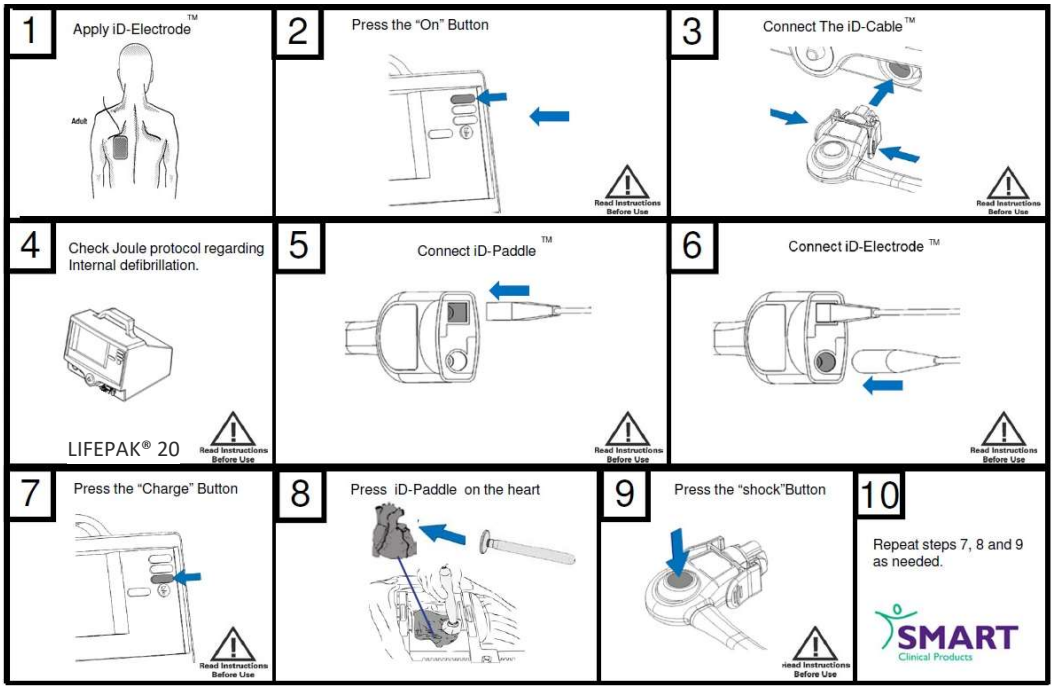

Figure 3: Instructions for use of the iD-System.

When ventricular fibrillation of ventricular tachycardia occurs, the iD-Paddle will be applied directly to the heart. (figure 1: step 1-10)

The surgeon selects the right amount of Joules, with a maximum of 50 Joules, conform to the defibrillator 'LIFEPAK 20®'. The device may only be used by medical specialist and nurses, in the operating area. In case of internal defibrillation, extra questions (attachment 4) focused on efficacy will be filled in by the surgeon. We hypothesize that in 10% of the study population, thus 10 patients (out of 100), ventricular fibrillation or tachycardia will occur. In this small subpopulation, the ease of use of the iD-Paddle and the efficacy can be tested. In case that this number is not reached, the ease of use of the iD-Paddle can be tested without defibrillating the patient. We will then connect the iD-Paddle to the iD-Cable and press the iD-Paddle on the heart without pressing the 'charge' and 'shock' button.

In case ventricular fibrillation occurs and the iD-System is not effective to restore the sinus rhythm, the conventional approach with use of the two paddles spoons will be performed. One paddle is placed behind the left ventricle, and the other is positioned over the right ventricle on the anterior surface of the heart, with current flowing directly through the heart.

During surgery, all patients are monitored to observe possible abnormalities on ECG. As part of standard of care, blood samples are taken at certain time points to measure myocardial damage (troponin-T).

The suspected workflow is the following:

- Pre-operative: evaluate inclusion- and exclusion criteria → ask for informed consent when meeting the criteria
- Per- operative:
    - Baseline: blood sample (standard of care)
    - apply the iD-Electrode on the patient's back
    - connect the iD-Cable to the LIFEPAK 20 defibrillator
    - connect the iD-Electrode and the iD-Paddle to the iD-Cable
    - **IF** defibrillation occurs: figure 4

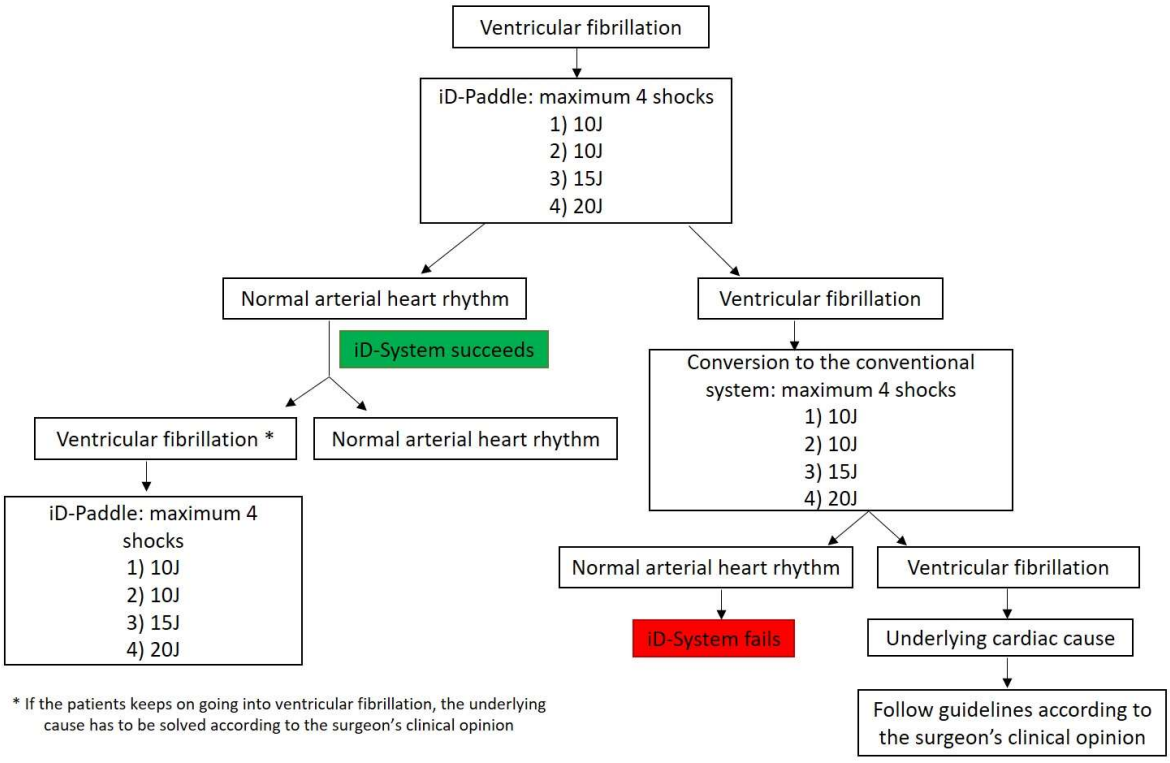

Figure 4: flow chart of internal defibrillation with the iD-System and, when needed, with the conventional system.

- Post-operative:
    - Questionnaire 'safety' filled in by the surgeons who handled the device
    - **IF** defibrillation occurs: questionnaire 'efficacy' filled in by the surgeons who performed defibrillation with the iD-Paddle
    - For every patient: patient characteristics + small report of the surgery based on some questions
    - Blood sample: troponin T (standard of care)
        - 4 – 8 – 16 – 24 – 36 hours

5.3. **Withdrawal from the study**

As stated in the informed consent form, patients can choose to withdraw from the study at any time and for any reason without any consequences.

6. SAFETY AND COMPLIANCE

6.1. **Adverse events and serious adverse events**

Every adverse event (AE) defined as any undesirable experience occurring to a subject during a clinical trial, will be reported. No diagnosis will be made, no treatment will be initiated and no medical decision will be taken based on the investigated biomarker testing. In this study, the occurrence of AEs / SAEs will therefore be considered unrelated to the investigated biomarkers. Therefore no indirect harm related to the investigated POC assay in the context of this study.

A 'serious adverse event' (SAE) is every medical occurrence or effect that results in:

- death
- life threatening situation
- hospitalization or prolongation of existing in patients' hospitalization
- persistent or significant disability or incapacity
- any other medical significant occurrence

6.2. **Compliance statements**

The study will be conducted in compliance to this study protocol, the current version of the Declaration of Helsinki, ICH GCP, and applicable local legal and regulatory requirements.

Sufficient insurance coverage according to legal requirements for subjects participating in the study is ensured. Subjects will be informed about this and will be asked to inform the assigned investigator about any harm they believe to be associated with their participation in this study.

Auditors, Ethics Committee, and the regulatory authorities will be granted direct access to the subject's medical records to the extent permitted by the applicable law and regulation for verification of clinical study procedures, and/or data control, ensuring subject data confidentiality. The subject's file and the source data will be archived in line with national and international legal requirements.

The results of the clinical study will be documented in a clinical study report and if possible, will be published (e.g. in a journal or presented in a scientific meeting).

7. STATISTICAL ANALYSIS

As the study is mainly observational, no in-depth statistical analysis will be used. However, the patient population will be described via column statistics or contingency tables.

8. REFERENCES

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9. ATTACHMENTS

Attachment 1

Clinical evaluation plan of the product

Attachment 2

Brochure of the iD-System™, One-handed Disposable Internal Defibrillation System

Attachment 3

Report of the biotechnical department

Attachment 3.1

Scan of measurement 16, 17 and 18 for verification of the report

Attachment 4

Questionnaire about safety and efficacy of the iD-System