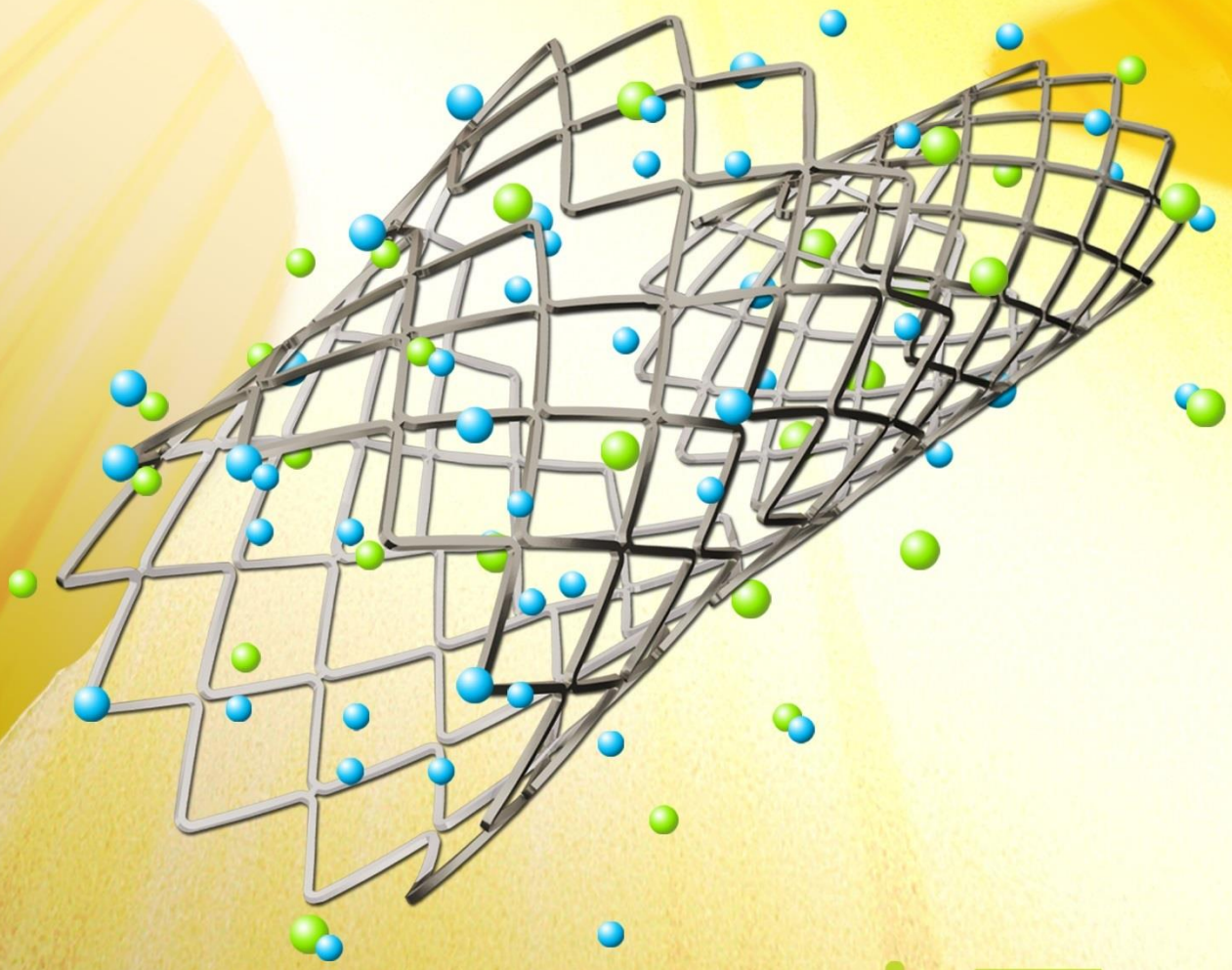
Nile®

Sir

Sirolimus Elution

CLINICAL DATA



MINVASYS

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1 INTRODUCTION

Coronary bifurcations account for 15-20% of all percutaneous coronary interventions and remain one of the most challenging lesions in interventional cardiology in terms of procedural success rate as well as long-term cardiac events. Furthermore, Stent Thrombosis (ST) at coronary bifurcations may jeopardize a greater territory of myocardium at risk and potentially increase the risk of adverse cardiovascular outcomes [1]. Bifurcation geometry (the angle between the main branch and the side branch), assessment of lesion severity, vessel location, bifurcation classification, type of stent, stenting technique and residual stenosis are some of the important issues that need to be considered when dealing with a bifurcation lesion [2].

Despite advances in Percutaneous Coronary Intervention (PCI) techniques and the introduction of Drug-Eluting Stent (DES), bifurcation lesions continue to be associated with higher revascularization rates as compared to non-bifurcation lesions [3] and increased risk of ST, ranging from 1% to 3% at mean follow-up of 10 months in randomized studies of bifurcation stenting [4] [5].

The continuous development of novel technologies, dedicated bifurcation stents and use of more appropriate strategies may contribute to have safer and better outcomes in patients with bifurcated lesions.

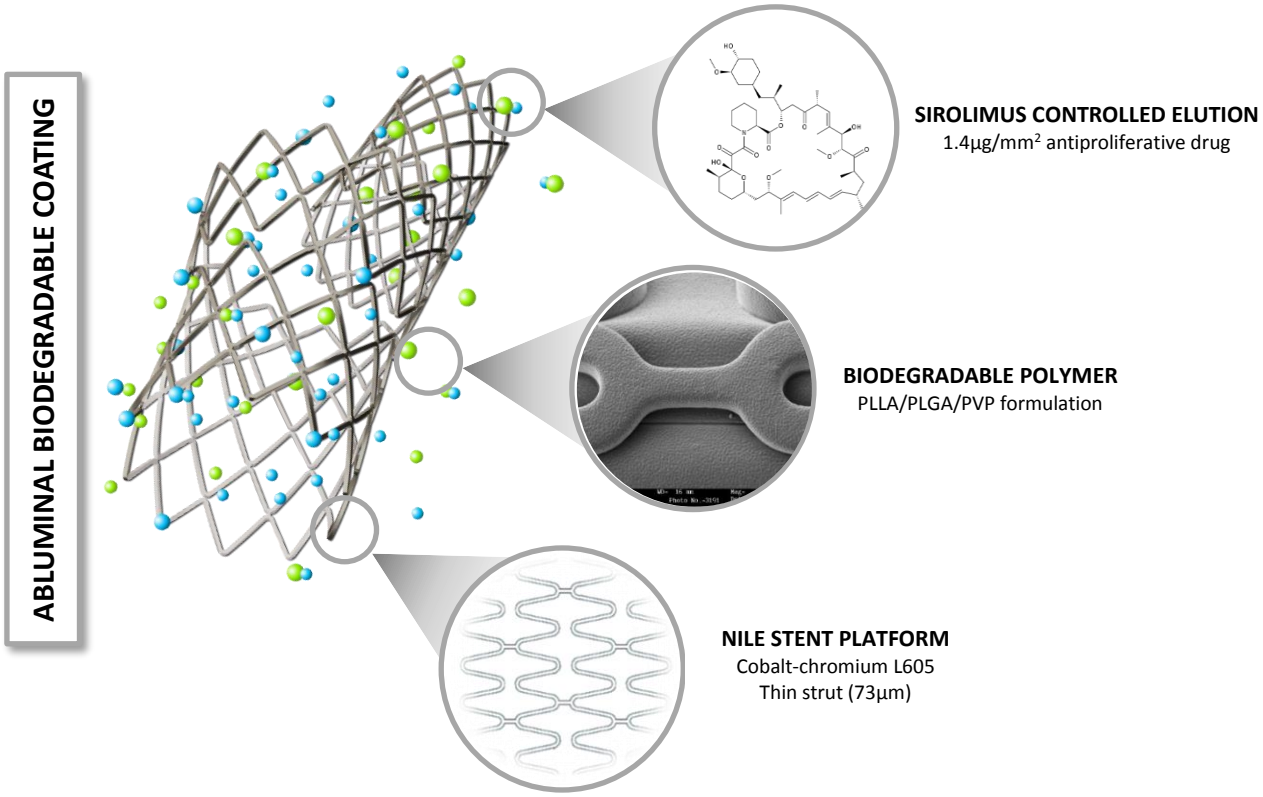
In the past few years, various clinical studies have evaluated the safety and efficacy of the use of DES, Biodegradable Polymer (BP) DES and dedicated stents for the treatment of bifurcation coronary artery lesions.

MINVASYS developed the Nile SIR, a Sirolimus-Eluting Stent (SES) with Biodegradable-Polymer (BP) matrix dedicated to the treatment of coronary bifurcation artery diseases.

The safety and efficacy of the Nile SIR device were evaluated through a first-in-man study that will be presented hereafter.

2 DEVICE DESCRIPTION

The Nile SIR is a biodegradable polymer based drug eluting coronary dedicated stent. The device includes three main components:



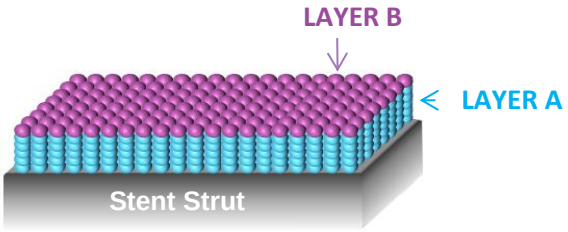
Anti-proliferative drug - Sirolimus

The device coating is a combination of inactive and active component. The active component is an anti-proliferative drug, sirolimus. Sirolimus also known as rapamycin, is an immunosuppressant drug that prevents activation of T cells and B-cells by inhibiting their response to interleukin-2 (IL-2).

The anti-proliferative effect of sirolimus prevent restenosis in coronary arteries. Sirolimus is formulated in blend of polymer coating that provides controlled release for a longer duration post coronary intervention.

Biodegradable polymers

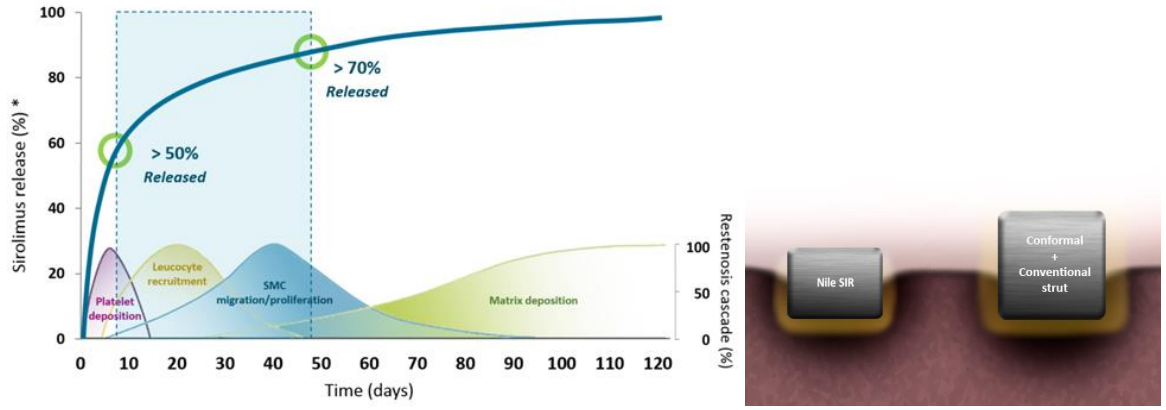
The inactive component is a Poly L-lactide based family of polymer (biodegradable and biocompatible polymer) which is released with the drug and degrades after 6 to 8 months.



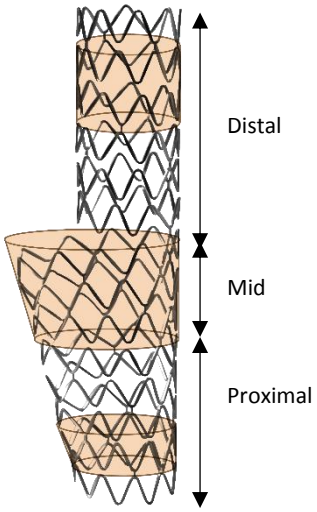
LAYER A - **Sirolimus drug** and **Poly-L lactic Acid** (PLLA), **Poly(lactic-co-glycolic) acid** (PLGA), **Polyvinylpyrrolidone** (PVP)
Bio-absorbable, biocompatible and non-toxic polymers.
LAYER B- **Poly Vinyl Pyrrolidone** (PVP)
100% Protective layer without drug. Biodegradable, water soluble polymer

Sirolimus controlled elution

The combination of two layers coating technology and abluminal drug distribution ensure an effective and controlled elution of sirolimus to arterial wall, and therefore perfectly adapted to prevent natural adverse effects of healing process.



Stent platform



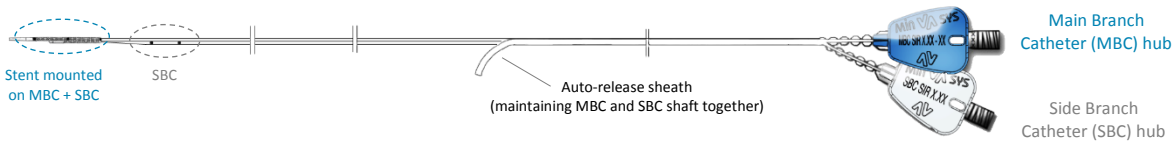
The Nile SIR stent platform is a cobalt-chromium alloy (L605) stent designed with a low strut thickness (73µm). The stent platform is dedicated to bifurcated lesions and is designed with a single link at the level of the carina to prevent Side Branch (SB) obstruction.

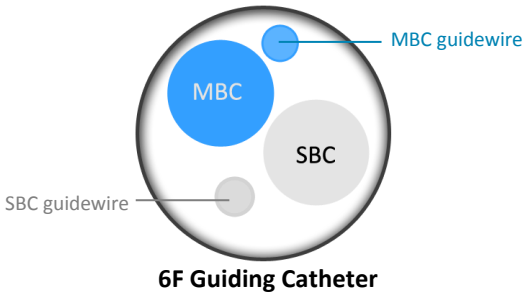
The dedicated design ensures a same metal/artery ratio all along the bifurcation artery without cell overstretching:

- 6 or 8 cells on the distal part
- 8 or 10 cells on the carina
- 7 or 9 cells on proximal part

Catheter system

The Nile SIR stent is mounted on an extra-thin dedicated Stent Delivery System (SDS), made of two parallel rapid exchange (RX) catheters designed for transluminal angioplasty by percutaneous way and adapted to bifurcation morphology: the Main Branch Catheter (MBC) and Side Branch Catheter (SBC).





6F Guiding Catheter

Nile SIR MBC is used as a stent carrier. This catheter includes distally two coaxial lumens.

The MBC is provided with two types of markers: radio-opaque (3: proximally, at the level of the ostium and distally) and visual markers (2 at the proximal shaft).

Nile SIR SBC is used to access SB vessel for post-dilatation. As per MBC, this catheter includes distally two coaxial lumens.

The SBC is provided two types of markers: radio-opaque (2; proximally and distally) and visual (2; at the proximal shaft).

3 First-in-man evaluation of the Nile SIR stent

AIM

The purpose of the present study is to capture the clinical results of patients receiving the Nile SIR dedicated stent with sirolimus drug and biodegradable polymer matrix on cobalt-chromium platform.

METHODS

Between June 2013 and July 2014, 37 patients with symptomatic coronary bifurcation artery diseases were treated with the Nile SIR drug eluting dedicated stent in India. The objective of this prospective multicenter, first-in-man clinical trial was to assess the safety and efficacy of the Nile SIR for the treatment of native coronary bifurcation arteries. The study endpoints were the angiographic and procedural success and MACE rate at 1, 3, 6 and 12 months follow-ups.

A subgroup of patients had an angiographic control between 6 and 12 months.

Patients' demographic data are presented hereafter:

POPULATION	
Patient, n	37
Age, years	59.7±9.1
Male, %	78.4
CLINICAL INDICATION	
Stable angina, %	64.9
Unstable angina, %	35.1
RISK FACTORS	
Hypertension, %	43.2
Dyslipidemia, %	10.8
Insulin-dependent diabetes, %	37.8
Current smoker, %	5.4
Previous MI, %	29.7
Family history of CAD, %	10.8
Renal insufficiency, %	2.7

LESIONS CHARACTERISTICS		
	MB_p-MB_d	**SB**
Lesion treated, n	38	
Lesion length, mm	16.0±8.9	8.9±5.5
Reference Diameter, mm	2.7±0.4	2.0±0.5
- $MB_{proximal}$, mm	3.2±0.5	-
- MB_{distal}, mm	2.5±0.6	-
MLD, mm	1.0±0.4	1.2±0.5
Percent DS, %	62.5±14.2	39.9±24.7
Medina classification, %		
- 1-1-1	24	
- 1-1-0	13	
- 1-0-1	11	
- 0-1-1	13	
- 1-0-0	24	
- 0-1-0	8	
- 0-0-1	8	
Target vessel, %		
- LAD/Dg	74	
- LCx/OM	26	
- RCA-PDA/PLSA	0	
- LMCA	0	

RESULTS

Procedural data

There were 38 lesions treated with a mean lesion length of 16.0±8.9mm in the Main Branch (MB) and 8.9±5.5 in the Side Branch (SB). The Reference Vessel Diameter (RVD) was 2.7±0.4mm in the MB and 2.0±0.5mm in the SB.

The main branch was predilated in 84% of patients and the side branch in 50% of patient. 34% of patients received a stent in the SB and post-dilatation was performed in 45% in the MB and 29% in the SB. Kissing balloon inflation was done in 63% of patient. 27% of patients received an additional stent in the MB and 3% in the SB.

There were no procedure complications and no adverse cardiac events at discharge.

Clinical follow-up results

All patients were clinically followed by phone call or visit at the hospital. Up to 6 months post-procedure, there were no reported major adverse cardiovascular events (including myocardial infarction, target lesion revascularization and cardiac death). There were three non-cardiac deaths reported up to 12 months.

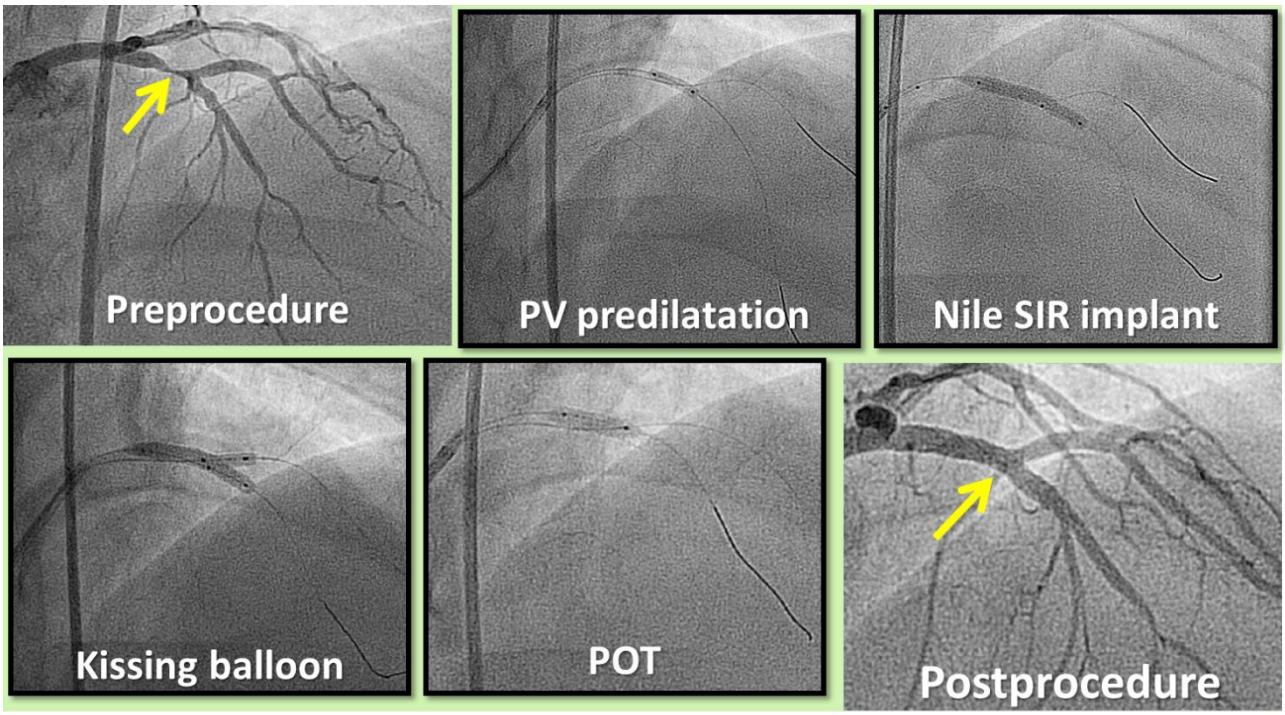
Angiographic follow-up at 6/12 months

Angiographic control between 6 and 12 months post-procedure was performed in 15 patients. For angiographic outcomes see Table 1.

Table 1: Angiographic results in 15 patients

	$MB_{proximal}$	MB_{distal}	SB
In-segment			
- RVD, mm	2.97 ± 0.48	2.45 ± 0.39	2.13 ± 0.70
- Mean diameter, mm	3.04 ± 0.41	2.43 ± 0.34	2.17 ± 0.51
- MLD, mm	2.44 ± 0.32	2.07 ± 0.39	1.73 ± 0.51
- % DS	16.6 ± 11.0	15.1 ± 10.0	18.1 ± 3.7
- LLL, mm	0.15 ± 0.15	0.10 ± 0.27	0.08 ± 0.21
In-stent			***Ostium***
- RVD, mm	2.55 ± 0.33	2.55 ± 0.32	2.17 ± 0.52
- Mean diameter, mm	2.76 ± 0.29	2.52 ± 0.34	2.14 ± 0.43
- MLD, mm	2.47 ± 0.34	2.23 ± 0.30	1.76 ± 0.39
- % DS	19.3 ± 12.2	11.7 ± 11.4	18.3 ± 7.2
- LLL, mm	0.20 ± 0.16	0.16 ± 0.29	0.26 ± 0.41

PATIENT CASE



CONCLUSION

In this Nile SIR first-in-man clinical trial, there were no safety concerns up to 6 months. Indeed, there were no reported major cardiac adverse event. Moreover, the angiographic follow-up results between 6 and 12 months were excellent, with a measure of in-segment late lumen loss of 0.15±0.15 mm in the $MB_{proximal}$, 0.10±0.27 mm in the MB_{distal} and 0.08±0.21 in the SB.

This Nile SIR study is a first-in-man clinical evaluation and therefore is limited by a small patient cohort. Long-term safety and effectiveness of the Nile SIR biodegradable polymer dedicated stent will be confirmed in a larger cohort registry.

4 REFERENCES

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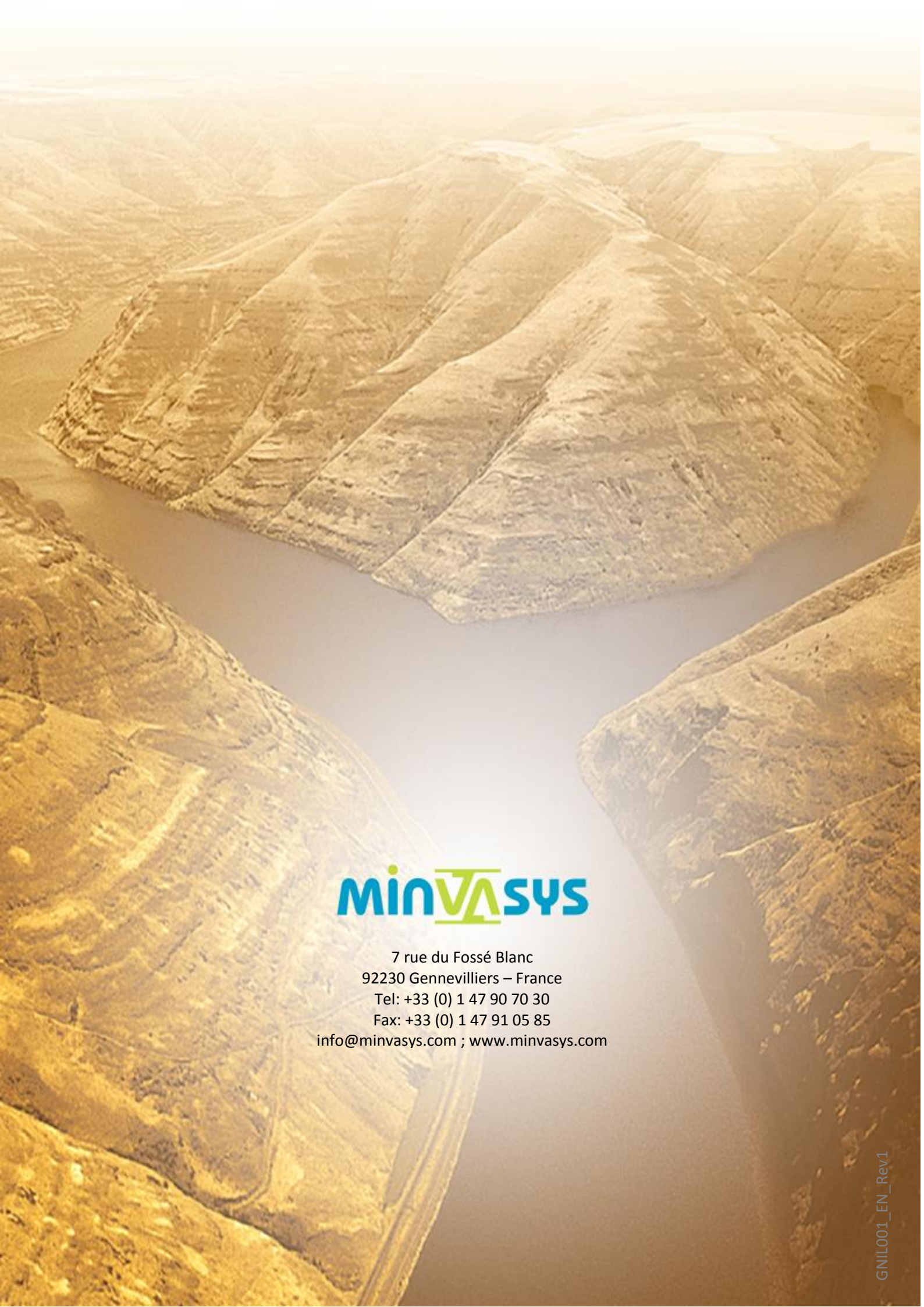

7 rue du Fossé Blanc
92230 Gennevilliers – France
Tel: +33 (0) 1 47 90 70 30
Fax: +33 (0) 1 47 91 05 85
info@minvasys.com ; www.minvasys.com

GNIL001_EN_Rev1