CHAPTER 1

GENERAL INTRODUCTION, AIMS AND OUTLINE OF THE THESIS
Worldwide caesarean birth rates are rising. In the United Kingdom the caesarean section (CS) rate increased from 12 to 29% between 1990 and 2008. In the USA in 2011 one in three women delivered by CS, whereas in China the CS rates have even risen from 2% in 1985 to 36–58% in 2010 and in Brazil from 15% in 1970 to even 80% in the private sector in 2004. There is no doubt that when a CS is performed for a medical or emergent reason, it can prevent maternal and new-born mortality. But with rising numbers of CS, the maternal morbidity including complications increases while new-born outcomes do not improve.

The World Health Organisation stated in 2015 that CS rates above 10% at a population level are not associated with decreased maternal and new-born mortality. In 2010 the world health organisation obtained data of the CS rates from 137 countries, which accounted for 95% of global births and reported that 14 of 137 countries had a CS rate of 10-15% and 69 of 137 countries had a CS rate >15%. The latter group accounted for a total of 6.2 million unnecessary CSs per year. Besides logically the high costs for public healthcare services of all these unnecessary CSs and the increased peripartum mortality and morbidity, CSs are associated with long term complaints and obstetric risks as well, which can affect the mother or child or can cause problems in future pregnancies.

**THE NICHE**

Already in 1999 it was postulated that long term gynaecological symptoms after CS might be related to a niche. A niche is an indentation at the site of the caesarean scar in the uterine wall. In approximately 60% of women a niche with a minimal depth of 2 mm is seen with sonohysterography 3-12 months after CS. A niche can be visualised with the use of transvaginal ultrasound, sonohysterography or hysteroscopy. However, studies reported sonohysterography to be the most accurate method to identify and measure a niche. Small niches, that can also cause spotting, can be missed using transvaginal sonography without contrast. A niche can be measured in the sagittal plane where the niche has the largest depth and the thinnest residual myometrium (Figure 1a). In this sagittal

![Diagram of a niche](image)

**Figure 1a-b Measurement of the niche**

a. A: Length (red line) B: Depth (green line) C: Residual myometrium (blue line)

b. A: Width (grey line)
plane where the niche is largest, the width of the niche can be measured in the transversal plane as well (Figure 1b). The depth and residual myometrium of eventual thin lateral branches in the niche can be measured separately.

Niche related symptoms and possible risks

A niche, and in particular large niches have been associated with gynaecological complaints such as postmenstrual spotting, dysmenorrhea, pelvic pain or dyspareunia.\textsuperscript{10-12, 14, 15} Two independent cohort studies reported that postmenstrual spotting occurs in approximately 30\% of women with a niche, in comparison to approximately 15\% of women without a niche after CS.\textsuperscript{11, 12} The etiology of niche related postmenstrual spotting and pain has not been fully elucidated. It is thought to be caused by retention of menstrual blood in a niche, which is intermittently expelled after the majority of the menstruation has ceased. Blood can also accumulate, if fibrotic tissue in the myometrium at the site of the caesarean scar may impair normal contractions and as a consequence the drainage of menstrual flow. Additionally, newly formed fragile vessels in the niche may also attribute to the accumulation of blood or fluid in the niche or uterine cavity due to a constant low production of in situ leakage of blood and fluid. Pelvic pain complaints and dyspareunia may in theory be a result of the manipulation of (strong) intra-abdominal adhesions which are often found after CS between the uterine wall at the site of the caesarean scar/niche, the bladder and/or the abdominal wall.\textsuperscript{16-18} In addition to the gynaecological symptoms niches may impair subsequent fertility. Intrauterine fluid during the ovulation, or mucus and blood accumulation in the cervix in association with a niche may hamper the penetration of sperm cells or impair embryo implantation.\textsuperscript{19, 20} Furthermore, a (large) niche can cause inaccessibility to the uterine cavity due to a distorted anatomy of the uterus in particular in combination with strong retroflexion of the uterus, causing problems during intra-uterine insemination or embryo transfer. A CS on average reduces the probability of a subsequent pregnancy by 4-19\%.\textsuperscript{21, 22} The size of the effect depends on the type and indication for CS, but even if the true reduction in fertility would be closer to 4\% than to 19\%, this has high impact in view of the high numbers of CS performed globally. An eventual relationship between subfertility and a niche has not been studied yet. At last, a niche can cause (life threatening) complications during pregnancy, such as a caesarean scar pregnancy, malplacentation and possibly an increased risk of a failed trial of labour resulting in an intrapartum (emergency) CS.\textsuperscript{23-30}

Treatment of niche related symptoms

First of all, it is important to realise that not all niches cause complaints which means these niches do not need any treatment. In women with bothersome niche related symptoms, medical or surgical therapy can be considered.\textsuperscript{31} Hormonal medication or a levonorgestrel IUD can be offered to women who have no desire to conceive. However, a few studies reported that niche related menstrual bleeding disorders or cyclic pain do often not respond to hormonal therapies, but comments can be made concerning the methodology of these studies.\textsuperscript{32, 33} Some authors have recommended hysterectomy as a treatment for niche
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related bleeding complaints in women without the desire to conceive, but the exact number of patients undergoing a hysterectomy due to niche related bleeding disorders is yet unknown. For women who do have the desire to conceive or the desire to preserve their uterus, a hysteroscopic or laparoscopic niche resection can be proposed.

A hysteroscopic niche resection (Figure 2a) has been described to treat niche related spotting symptoms and pain in women with a small niche with a residual myometrium of ≥ 2.5- 4.0 mm. The distal (and/or in some studies the proximal) rim of the niche is dissected hysteroscopicly and fragile vessels in the niche are coagulated with a rollerball.

At the start of this thesis reported previous cohort studies a reduction of postmenstrual spotting in 80-90% and a reduction in pain in 97% of the women at an absent complication rate. The mean reduction in the number of spotting compared to baseline was reported in two studies and varied between 2 to 4 days in 119 women.

A laparoscopic niche resection (Figure 2b) can be performed in women with a large symptomatic niche (residual myometrium of < 3 mm). In these women, a hysteroscopic resection might have a higher risk on bladder injury. In short, the niche is completely excised laparoscopically and the uterotomy wound is sutured in a double layer.

Earlier studies reported a reduction or complete resolution of spotting and pelvic pain and/ or dysmenorrhea to be dissolved after the niche resection. The residual myometrial thickness was increased after laparoscopic niche resection in all studies. The laparoscopic niche resection has also been performed as an experimental treatment for women with a large niche and secondary subfertility after CS. One study, including 18 secondary subfertile women with a niche, reported a pregnancy rate of 60% with a median time to conceive of 9 months after the niche resection.

All studies reporting on hysteroscopic or laparoscopic niche resection were not randomised or did not compare outcomes to expectant management, most studies had a small sample size, uniform definitions for the niche or postmenstrual spotting were not used, the studies did not use or mention (validated) tools to measure outcomes, outcomes were mostly not reported in a structural manner and few studies compared niche measurements at follow-up to baseline. However, surgical interventions to treat niche related symptoms are
performed more and more frequently in daily practice, despite the fact that the effectivity of these treatments has not been investigated properly. It is important to study the effectiveness of surgical interventions to treat niche related symptoms before they are implemented in daily practice.

AIMS OF THIS THESIS
The aims of this thesis were to answer the following questions:
1. What are the treatment options for niche related symptoms?
2. What is the safety and effect of a hysteroscopic niche resection on postmenstrual spotting in comparison with expectant management?
3. What is the effect of a laparoscopic niche resection of large niches on niche related symptoms?
4. What are the long term and reproductive outcomes after a laparoscopic niche resection?
5. What is the best timing for the implementation of laparoscopic niche resections?

OUTLINE OF THE THESIS
In this thesis the effect and implementation of minimal invasive treatment methods for niche related symptoms are evaluated. Based on the observations made during the studies included in this thesis we postulated some hypotheses on niche development. At the end, the thesis is discussed in general and a summary of the thesis is given.

In Chapter 2 we described a systematic review of the literature regarding current minimally invasive techniques to treat niche related symptoms.

In Chapter 3 we described the study protocol of the HysNiche trial, a randomised controlled trial that evaluates the effectiveness of the hysteroscopic niche resection on postmenstrual spotting in comparison to expectant management.

In Chapter 4 we studied the effect of a hysteroscopic niche resection on postmenstrual spotting in comparison to expectant management in a randomised controlled trial (HysNiche trial) and reported the results after six months follow-up.

In Chapter 5 we described the technique of the laparoscopic niche resection in a step-by-step tutorial to open a discussion on various technical aspects of the intervention in order to improve the technique of this novel surgical procedure.

In Chapter 6 we studied the effect of a laparoscopic niche resection on niche related symptoms in a prospective cohort study (LapNiche study) and reported the six months follow-up.

In Chapter 7 we presented the twelve months follow-up and reproductive outcomes of the LapNiche study.
In *Chapter 8* we classified the laparoscopic niche resection according to the IDEAL framework of ‘innovation stages’ and assigned the intervention a current research stage to be able to facilitate safe but properly timed implementation of this novel surgical technique.

In *Chapter 9* we hypothesised on the etiology of niche development based on the observations made during sonographic, hysteroscopic and laparoscopic evaluations of niches.

*Chapter 10* provides a general discussion of this thesis and presents future perspectives.

In *Chapter 11* an English and Dutch summary of this thesis are presented.


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51. Klemm P, Koehler C, Mangler M, Schneider U, Schneider A. Laparoscopic and vaginal repair of uterine scar...