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Pressure-dependent hydrometra dimensions in hysteroscopy

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Abstract
Aim To investigate the relation between intrauterine pressures and volumes for virtual-reality-based surgical training in hysteroscopy.
Material and methods Ten fresh extirpated uteri were insufflated by commercial hysteroscopy pump and imaged by computer tomography (CT) under intrauterine air pressure in distension–collapse cycles between 0 , 20 (150 mmHg), and 0 kPa, performing a CT scan at every step at about 2.7 kPa (20 mmHg).
Results An initial threshold pressure to distend the cavity was avoided by introducing the insufflation tube up to the fundus. The filling and release phases of seven uteri that were completely distended showed the typical characteristics of a hysteresis curve which is expected from a viscoelastic, nonlinear, anisotropic soft tissue organ like the uterus. In three cases tightening the extirpated uterus especially at the lateral resection lines caused significant problems that inhibited registration of a complete distension–collapse cycle. Interpolated volumes for complete distended cavities and extrapolated for incomplete data sets, derived from the digitally reconstructed three-dimensional (3D) geometries, ranged from 0.6 to 11.4 mL at 20 kPa. These values highly correlate with the uterine volume (not insufflated) considering different biometric data of the uteri and patient data. Linear ($R^2 = 0.66$) and quadratic least-squares fits ($R^2 = 0.74$) were used to derive the formulas $y = 0.069x$ and $y = 0.00037x^2 + 0.036x$, where x is the uterine volume in mL (not insufflated) and y is the cavity volume in mL at 20 kPa intrauterine pressure.
Conclusions Our experimental hysteroscopical setup enabled us to reconstruct the changes in volumes of insufflated uteri under highly realistic conditions in 3D. The relation between intrauterine pressure and cavity volume in distension–collapse cycles describes a typical hysteresis curve.

Keywords Hysteroscopy · Virtual-reality simulation · Volume · Pressure · Hydrometra · CT

In order to offer safe and efficient hysteroscopic interventions to patients, intensive training is required. Hysteroscopy represents the second most often performed minimally invasive group of interventions in gynecology. While high-fidelity virtual reality (VR)-based training for hysteroscopy is still under evaluation [1], synthetic and animal substitutes of the uterus are used for in vitro training purposes [2, 3]. VR-based endoscopic simulators have proven to provide a realistic, risk-free, and configurable training environment without any restriction for repetitive training on various anatomies and pathologies [4, 5].

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To access the uterine cavity, liquid or gas is filled until a defined maximal pressure is reached, commonly set between 16 kPa (120 mmHg) and 20 kPa (150 mmHg). During interventions, intrauterine pressure changes are remarkable, either deliberately altered by the valves on the hysteroscope or uncontrolled through liquid or gas losses through natural or artificial openings.

A realistic impression during virtual training on a simulator therefore greatly depends, amongst other factors, on correct elastomechanical behavior of the computer model that captures different intrauterine pressure states. To the best of our knowledge, no digital three-dimensional (3D) description of hysteroscopy distended uterine cavities has been presented to date. Therefore, the aim of this feasibility study was to determine the 3D representation of uteri and their cavities in vitro at different intrauterine pressure stages typically used in hysteroscopy.

Material and Methods

Data was obtained from ten uteri of prospectively selected pre- and postmenopausal patients between 36 and 68 years old (Table 1). The women were subjected to hysterectomy between October and November 2005 exclusively for medical reasons. The study protocol was approved by the subcommission of the Ethical Board of the Canton Zurich (SPUK-GGU, Swiss Ethics), and informed written consent was obtained from all patients. Uteri with evidence of premalignancy or malignancy were excluded from the study. In order to focus the investigation on uteri with healthy myometrium, only uteri with no or small suspected leiomyomas that do not affect the cavity were chosen.

Directly after extirpation, uteri were stored in a refrigerator at 4–8°C, undergoing a warm-up phase in a water bath of 30°C directly before CT examination was started at 20°C. Time between start of surgery and start of CT ranged between 4 h 55 min and 10 h 15 min. Uteri 1–4 (series 1, Table 1) were connected to a commercial insufflator apparatus (2200 Hystero Pump, Richard Wolf GmbH, Knittlingen, Germany) via a polyvinyl chloride (PVC) lathed adapter (7 mm in diameter), substituting the hysteroscope. The adapter was inserted through the cervical channel only slightly beyond the internal opening in order to not distend the cavity. Uteri 5–10 (series 2, Table 1) were linked to the insufflator via a silicon tube (4 mm in diameter) containing small holes distributed over a length of 2 cm on the inserted tip. In this series, the tube was introduced further into the uterine cavity until it touched the fundus, deliberately separating the two endometrial layers. Subsequently, the cervical channel of all ten uteri was tightened over the transcervically placed insufflation adapter or tube respectively by a double cerclage of broad 4-mm cable ties.

If a fluid with the same viscosity as hydrotubation dye is used for distension, spillage at the fallopian tubes is expected at intrauterine pressures higher than 9.3 kPa (70 mmHg) [6]. Therefore, aiming at a top pressure of 20 kPa (150 mmHg), ligatures were placed routinely on the intramural part of both fallopian tubes before insufflation began. During the experiment, further ligatures were added wherever the distending media leaked, which predominantly occurred on both lateral insertion lines of the broad ligaments.

In order to achieve the highest contrast between the endometrium and the expanded uterine cavity, we tested a number of different imaging modalities. Both magnetic resonance imaging (MRI) and ultrasound equipment achieved only very low spatial resolution in our pilot studies. Using 0.9% NaCl and water as distension media did not provide sufficient contrast due to very similar linear attenuation coefficients to soft tissue. CT imaging and air

Table 1 Patient data

Uterus number	Series	Age (years)	Menopause status	Last period (dd/mm/yy)	Hormones (HRT, oral contraceptives, etc.)	Number of pregnancies	Number of deliveries	Uterine surgery in the past
1	1	56	Post	?	–	4	3	–
2	1	62	Post	?	–	2	2	–
3	1	36	Pre	19/09/05	–	1	1	D&C, HC
4	1	40	Pre	bleeding disorders	–	3	2	3 × D&C
5	2	46	Pre	20/10/05	–	3	2	D&C
6	2	43	Pre	01/09/05	–	2	2	D&C, HC
7	2	68	Post	01/01/79	–	3	3	–
8	2	48	Pre	31/05/05	–	2	2	–
9	2	66	Post	01/01/91	–	3	3	D&C
10	2	58	Pre	16/09/05	–	2	2	D&C

HRT hormone replacement therapy, *D&C* dilatation and curettage, *HC* hysteroscopy as distension media resulted in superior contrast between the distended uterine cavity and its surroundings, therefore enabling the most accurate reconstruction of the 3D geometry of the cavity at different stable pressure states. The resulting pressure in the uterine cavity is purely hydrostatic and therefore not distinguishable from a pressure generated by resting liquid.

Prior to each experiment, the hysteroscopy pump was calibrated with a mercury column and showed a maximum absolute error of 133 Pa (1 mmHg). The flow rate of the pump was set to the minimum possible level of 30 mL/min. The intrauterine pressure was consecutively increased from 0 to 20 kPa (150 mmHg) and subsequently decreased to 0 kPa by steps of about 2.7 kPa (20 mmHg). More specifically, the pressure was increased after a successful CT scan, whereupon the pump was turned off. Due to the viscoelastic properties of the uterus, the pressure then decreased by a few hundred Pascals. As soon as a stable pressure state was observed for at least 10 s and the CT system was idle after finishing the postprocessing of the last scan, the current pressure value was noted and complete CT scan of the uterus was performed. Each uterus underwent one distension–collapse cycle. Whenever a leakage occurred, the exact source was localized and the pressure was reduced to 0 kPa before adding further ligatures. To resume the experiment, the uterus was repositioned, pressure was applied, and measurements were taken at the pressure state at which leaking had occurred.

All scans were performed on a 16-row multidetector computer tomography Brilliance-16 scanner (Koninklijke Philips Electronics N.V., DA Best, The Netherlands) using the following parameters: tube voltage 90 kV, tube current 375 mAs/slice, slice collimation 16 mm $\times$ 0.75 mm, pitch 0.658. Slices with a thickness of 0.80 mm (increment 0.40 mm) and a medium soft tissue kernel (filter C) were used for evaluation.

Triangulated isosurfaces of the uteri were extracted from all datasets with Imaris 4.0.6 software (Bitplane AG, Zurich, Switzerland). Isosurfaces connect points of the same intensity in a volume to a triangular mesh by setting a threshold for the grey scale values provided by the scanner. For this study, the threshold value was set to 525, which is the arithmetic mean between 1,050 for myometrium and 0 for air (Fig. 1). In cases where the surface was not clearly separated from any of the other reconstructed objects, corrections were performed manually by a clinical expert. Pressure–volume data were graphically processed using Sigmaplot 10.0 (Systat Software Inc., San Jose, CA, USA) (Figs. 2, 3, 4). The volumes of the uterine cavities were determined with the software package Geomagic Studio 7 (Raindrop Geomagic Inc., Durham, NC, USA) (Figs. 5, 6). The error of the volume estimation resulting from the segmentation and spatial resolution limitations of the CT

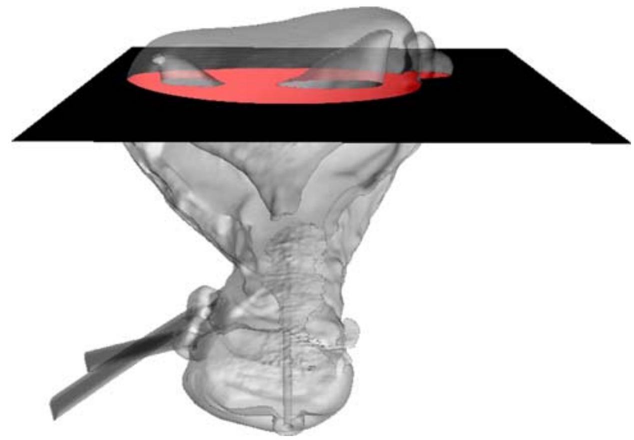

Fig. 1 Isosurface of uterus 3. The uterine surface as well as the surface of the extended cavity are shown in semitransparent modus. The cervix contains the PVC adapter and is sealed by two cable ties. In an exemplary CT cutting plane near the fundus, the inside of the uterus is marked in *red*, the outside in *black*

scanner was estimated for one measurement (uterus 1, Fig. 3). For this purpose, every isosurface was both shrunken and expanded orthogonally by 0.5 mm and the corresponding cavity volumes were derived.

Exponential functions were fitted to the pressure–volume data for the filling phase of the experiment using the least-squares method. The volumes at 20 kPa (150 mmHg) were either interpolated or extrapolated according to the fitting function using the software package Matlab 7, R14 SP3 (MathWorks Inc., Natick, MA, USA). Some biometric measures of the examined uteri (Table 2), patient age, and number of pregnancies and deliveries (Table 1) were correlated with intrauterine volume at 20 kPa by applying linear and quadratic least-squares fits passing through the origin using the statistical features in Microsoft Excel 2003 version 11.0 for Windows (Microsoft Corp., Redmond, WA, USA).

Results

In series 1, the lowest intrauterine hydrostatic pressure required for a clear uterine distension ranged from 7.7 to 9.2 kPa (58–69 mmHg) and in series 2 from 2.1 to 5.2 kPa (16–39 mmHg) (Table 3).

All intrauterine pressure–volume relations were nonlinear. A hysteresis curve can be clearly identified in most of the experiments (Fig. 2) as expected for viscoelastic, nonlinear, anisotropic soft tissue organs such as the uterus. The estimated maximal absolute error for the measurements analyzed for uterus 1 was 0.9 mL (Fig. 3).

The maximum intrauterine pressures that could be established ranged from 8.4 to 20.7 kPa (63 – 155 mmHg) and the corresponding cavity volumes measured from 0.5

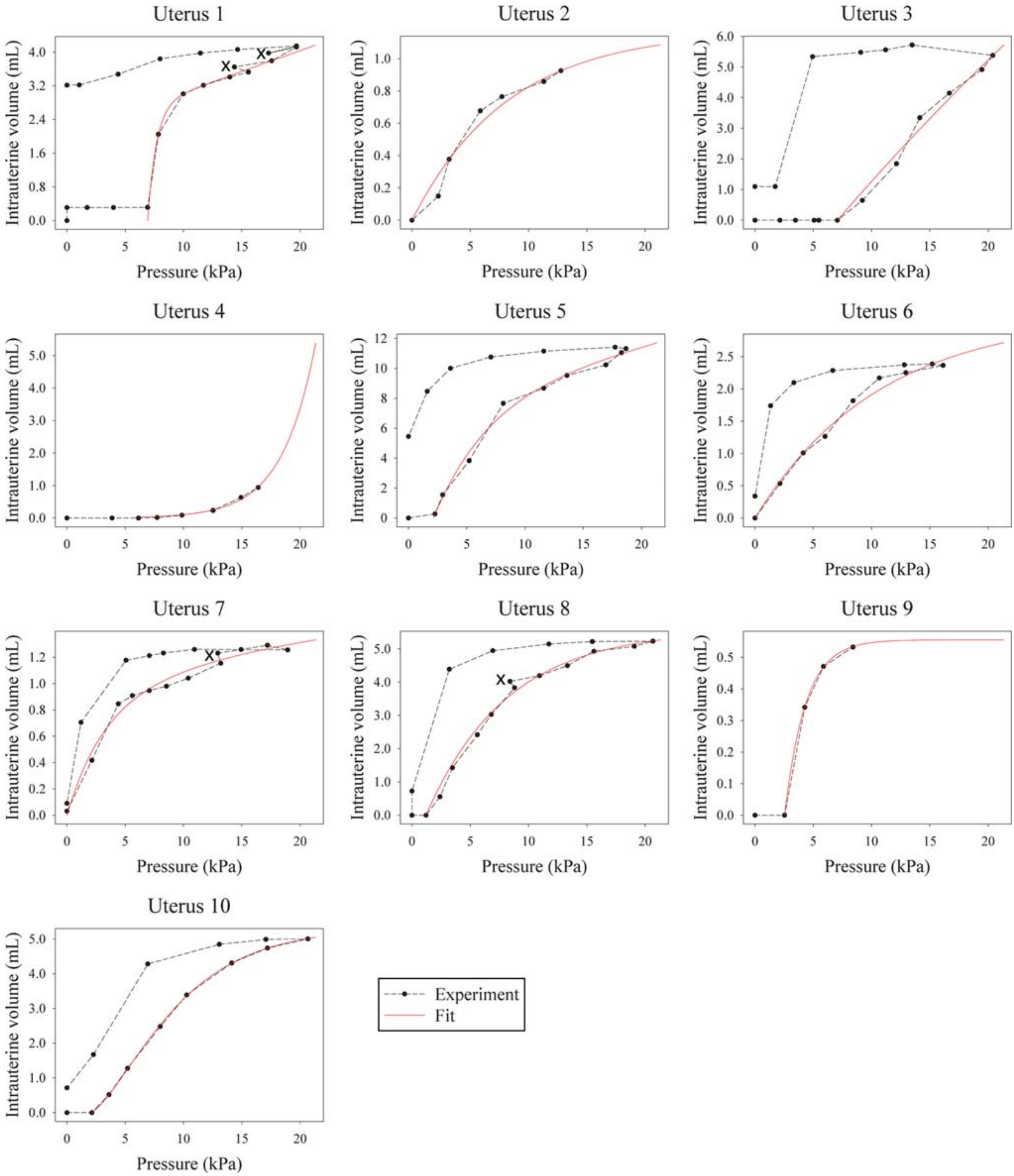

Fig. 2 Experimentally determined intrauterine volumes and the fitted curves to the filling phase for uterus 1–10. Uteri 1, 7, and 8 had to be sealed by additional ligatures when leakage occurred (uterus 1 at two different pressure states), marked by "x". After repair, maximum pressure could be applied. Uteri 2, 4, and 9 could not be sealed sufficiently by all efforts done and the experiment had to be truncated when the irreparable pressure leakage occurred, leading to incomplete hysteresis curves

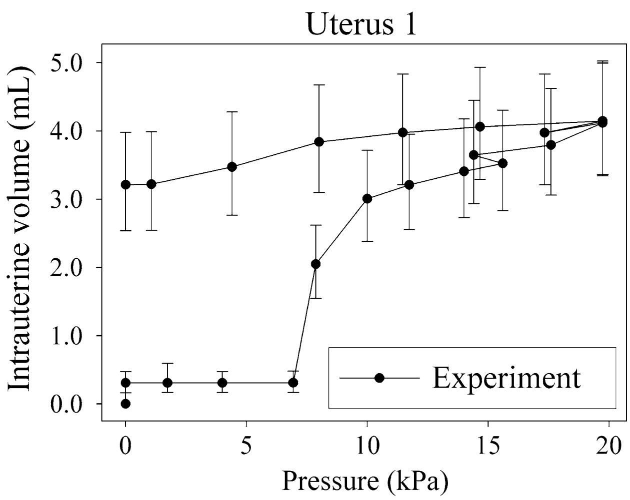

Fig. 3 Experimentally determined intrauterine volumes with vertical error bars representing the absolute volume errors of uterus 1 at different pressure states

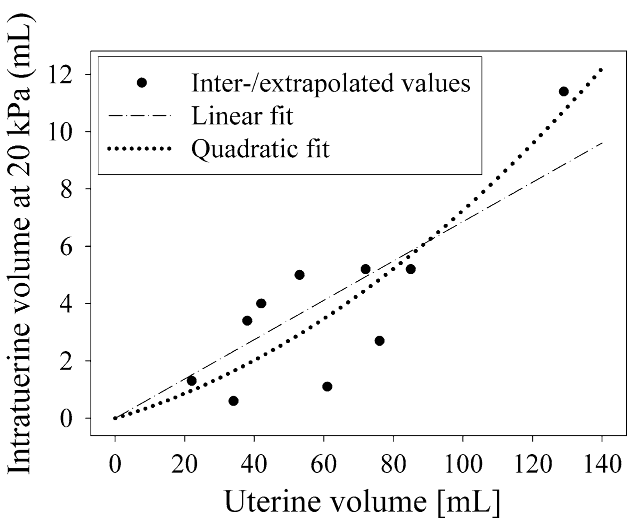

Fig. 4 Interpolated and extrapolated uterine cavity volumes at 20 kPa (150 mmHg) in relation to the uterine volume (not insufflated). Linear and quadratic fits are indicated by dashed lines

to 11.3 mL (Table 3). Three uteri (data sets 2, 4, and 9) could not be sealed sufficiently to apply the maximum pressure of 20 kPa (150 mmHg) despite the sealing efforts described above. Therefore, their cavity volumes were extrapolated for the pressure state of 20 kPa (150 mmHg). Interpolated and extrapolated volumes respectively under an intrauterine pressure of 20 kPa (150 mmHg) ranged from 0.6 to 11.4 mL (Table 3). The geometries of the maximally deformed cavities are shown dorsally in Fig. 5 and laterally in Fig. 6. Linear and quadratic least-squares fits between the interpolated and extrapolated cavity volumes at 20 kPa (150 mmHg), patient age, uterine volume, surface, length, corpus volume, corpus surface, corpus length, and total cavity length were performed. Thereby, the interpolated and extrapolated cavity volumes correlated best with the uterine volume (not insufflated) (Fig. 4). Linear ($R^2 = 0.66$) and quadratic functions ($R^2 = 0.74$) passing through the origin describing the relation between the uterine cavity volume at 20 kPa (150 mmHg) and the uterine volume have been estimated using least-squares fit, resulting in the following equations:

$$y = 0.069x, \quad (1)$$

$$y = 0.00037x^2 + 0.036x, \quad (2)$$

where x is the uterine volume in mL (not insufflated) and y is the cavity volume in mL at 20 kPa (150 mmHg).

Discussion

The presented in vitro study describes mathematically the relation between the intrauterine pressure and the corresponding intrauterine volume for a sample of ten nonpregnant human uteri in a setup similar to hysteroscopy, derived by CT measurements. To collect representative data comparable to a typical clinical set of cases undergoing surgery, only a few excluding criteria were defined (premalignancy or malignancy and cavity-deforming pathologies). In addition, patient data such as age, menopausal status, hormone therapy, number of pregnancies, number of deliveries, etc. were only recorded and did not influence the selection criteria. The acquired knowledge about the elastomechanical behavior of the uterus is essential, e.g., when building a realistic virtual-reality-based simulator for surgical training in hysteroscopy [7].

Anatomic attachments of the uterus are only located on both lateral sides of the corpus and the cervix, where the tight ligaments suspend the uterus in the lesser pelvis, allowing manifold enlargement, essential for human reproduction. Mazza et al. [8] performed repetitive aspiration cycles on cervices of human uteri and compared in vivo and ex vivo data from the same organ, measured approximately 1.5 h after extraction. Upon comparison of in vivo and ex vivo data they concluded that they did not differ considerably. Nevertheless, these authors found that the lack of perfusion might be a reason for the larger variability in the stiffness ex vivo (the tissue will not recover between tests as rapidly as in vivo). The load (pressure) is expected to be carried mainly by connective tissue and not by the muscle fibers [9]. As the experiments were conducted shortly after extirpation of the organs, post mortem changes were not expected to influence the results significantly. Therefore, we did not expect that extirpation of the uterus from the situs and insufflation by a relatively small amount of volume only a few hours after extirpation

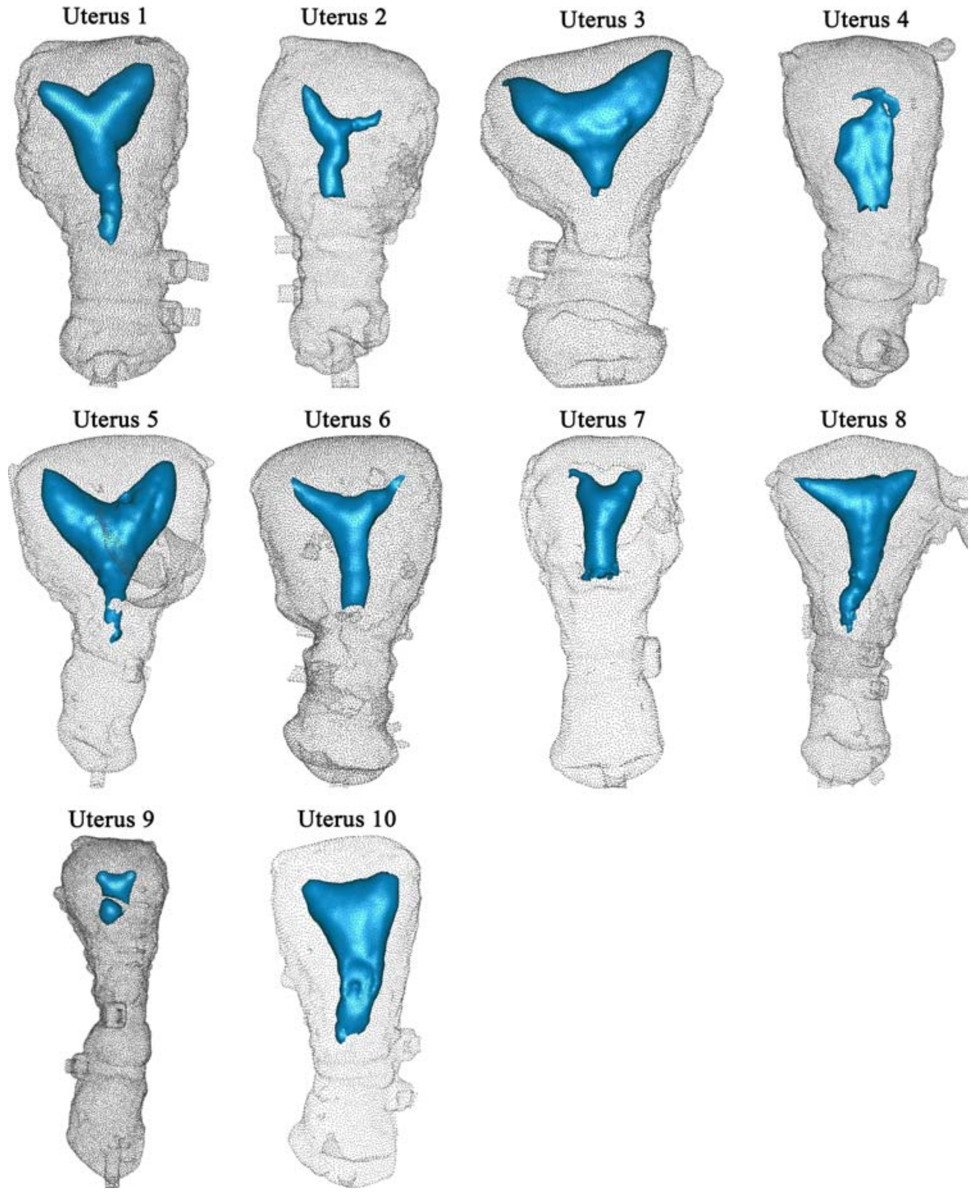

Fig. 5 Maximally deformed uterine cavities from dorsal (not to the same scale). Uterus surfaces are transparent and indicated by points

would create significant differences between ex vivo and in vivo examination.

In an earlier in vivo study [10], an initial minimum uterine pressure was required to distend the uterine cavity, with a median of 5.33 kPa (40 mmHg), ranging from 3.33 to 6.66 kPa (25–50 mmHg). The authors assumed that this phenomenon was a specific characteristic of the myometrium. Their in vivo results are in good agreement with the results from this study when the PVC adapter inserted through the cervical channel only slightly beyond the internal opening was used (series 1), which further supports the assumption that the post mortem changes did not affect the results substantially. However, in an earlier study investigating the three-dimensional fiber architecture of the uterus [11], we did not find any evidence for any morphologic substrate in the myometrial mesh which could be responsible for this behavior. We concluded that the explanation for the phenomenon of a minimal initial uterine pressure needed for dilatation would be due to adhesive forces between the two endometrial layers rather than an undetectable property of the myometrium. Therefore, we adapted the insufflation procedure for series 2 deliberately separating the two endometrial layers before insufflation was started. As Table 3 shows, the corresponding values in series 2 using a silicon tube introduced further into the uterine cavity until it touched the fundus were significantly lower, ranging from 2.1 to 5.2 kPa (16–39 mmHg). This difference clearly favors the hypothesis of adhesive forces between the two endometrial layers being responsible for an initial minimum pressure for cavity distension needed in series 1 and not the myometrium. Correct understanding of this phenomenon is essential for realistic hysteroscopy

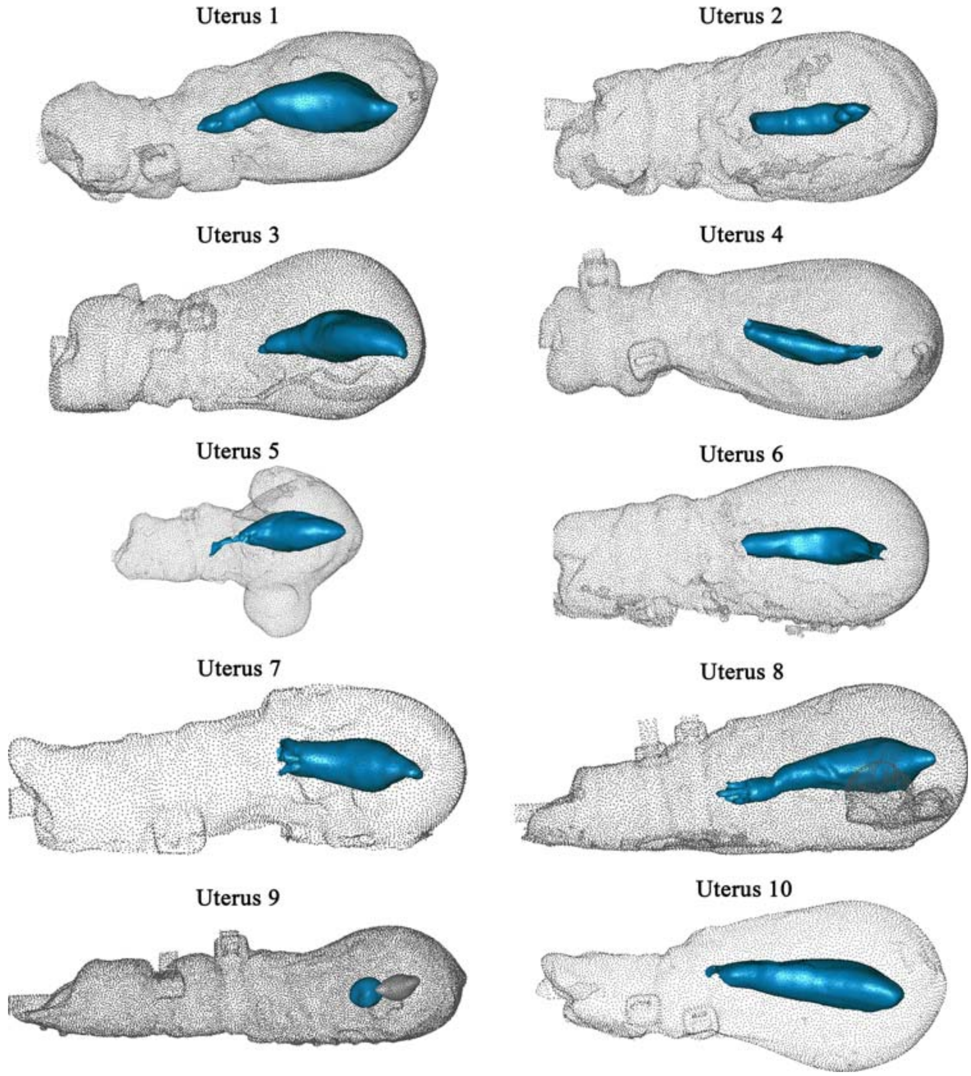

Fig. 6 Maximally deformed uterine cavities from the left side (not to the same scale). Uterus surfaces are transparent and indicated by points

Table 2 Biometric data of the ten uteri examined (not insufflated, series 1 uteri 1–4, series 2 uteri 5–10)

Uterus number	1	2	3	4	5	6	7	8	9	10
Uterus volume (mL)	42	61	72	38	129	76	22	85	34	53
Uterus surface (cm^2)	79	96	115	71	170	111	52	125	72	86
Uterus length (mm)	80	77	83	76	106	89	67	97	95	80
Corpus volume (mL)	31	46	49	28	103	58	15	69	21	45
Corpus surface (cm^2)	51	63	70	45	122	72	30	87	40	65
Corpus length (mm)	49	48	46	44	56	53	35	62	45	59
Cavity length, total (mm)	66	58	67	68	79	76	55	80	84	79

simulation and will significantly help us to simulate the initial phase of the hysteresis curve correctly.

The broad range of potential anatomies resulting from only applying a few selection criteria may explain the relatively high variability in our results; for example, the absolute volume errors are relatively high (Fig. 3). However, the characteristics of the pressure–volume curves found represent the expected hysteresis curve. It can be assumed that these curves are correct at least in a qualitative manner as all data sets for each individual uterus were segmented with the same algorithm and parameters. A distinctive hysteresis relationship between the intrauterine pressure and its volume has also been observed in dynamic in vivo experiments described in [12]. In contrast to these and our findings, Czekanowski et al. [13] reported a linear relation between intrauterine volume and pressure. They placed a latex balloon inside the uterine cavity and filled it with liquid in the range 0–20 mL. The volumes at 20 kPa (150 mmHg) pressure derived in this way varied between 2 and 18 mL (16 curves in chart, 21 examined uteri), i.e., substantially higher than the values presented here in the range 0.6–11.4 mL for the same pressure (ten examined uteri). We explain the latter difference primarily by the small number of cases in both studies.

Table 3 Pressure and volume values of the ten uteri examined (insufflated, series 1 uteri 1–4, series 2 uteri 5–10)

Uterus number	1	2	3	4	5	6	7	8	9	10
Maximum intrauterine pressure (kPa)	19.7	12.8	20.4	16.4	18.7	16.1	18.9	20.7	8.4	20.7
Cavity volume at maximum pressure (mL)	4.1	0.9	5.4	0.9	11.3	2.4	1.3	5.2	0.5	5.0
Interpolated or extrapolated volume at 150 mmHg (mL)	4.0	1.1*	5.2	3.4*	11.4	2.7	1.3	5.2	0.6*	5.0
Maximum pressure without clear cavity distension (kPa)	6.9	5.9	7.1	6.1	2.3	0.0	0.0	1.2	2.5	3.6
Minimum pressure for clear uterine distension (kPa)	7.9	7.7	9.2	7.7	2.9	2.1	2.1	2.4	4.3	5.2

Extrapolated volumes are marked by *

Corpus volume and uterine volume turned out to be the biometric measures of the examined uteri (Table 2) showing highest correlation with the interpolated and extrapolated cavity volumes at 20 kPa (150 mmHg) (Table 3) when relying on linear or quadratic least-squares models (Eqs. 1, 2). Especially the latter is more accurately defined and easier to determine. It has to be noted that single uteri significantly deviate from these relations.

After deflation some uteri showed lasting deformation. This might be due to slowly evolving time-dependent effects or due to irreversible (plastic) deformations in the uterine wall. It remains unclear to what extent this behavior was caused by the in vitro effect.

So far, only uteri with no or small leiomyomas not affecting the uterine cavity have been investigated. The influence of large uterine deformations due to pathologies on the relationship between intrauterine pressure and volume has to be analyzed in a next step, in order to complete hysteroscopy training on a variety of realistic surgical scenes. The presented data support our efforts to build a reference simulator for virtual-reality hysteroscopy on various anatomical models.

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