Investigation on the Behavior of κ-Carrageenan Hydrogels for Compressive Intra-Vessel Disintegration

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Gel disintegration via compression is a possible approach for the reversal of the occlusion of male vasa deferentia (VD) by hydrogels. κ-carrageenan (KC) hydrogels can be used for such an application. To determine the required forces for in-vessel compressive disintegration, a gel-tube model, preparing KC gels in different tubes, is studied. These gels are of alternating biopolymer (1–3% by mass) and potassium (100–300 mM) concentration. Gel-filled tubes are uniaxially compressed at two different compression speeds (1 and 0.3 mm s\(^{-1}\)). Breakage compression strains are cross studied by shear breaking gel measurements using dynamic mechanical analysis. The measurements showed good agreement. Gel structure disintegration occurred below (62 ± 8) % strain. During compression, three stages of gel disintegration are present. Gel-tube wall detachment, gel rupture, and gel expulsion. The force required for gel disintegration and tube deformation can be added arithmetically. From the modulus of a human aortae model, it is estimated that average human pinch forces are insufficient to disintegrate 2% and 3% by mass KC hydrogels in VD by massage. The compressive disintegration would require a compression device while evading tissue damage.

1. Introduction

Hydrogels from algae extracts are widely studied for tissue engineering and food applications.\(^1\) Studies of the mechanical gel disintegration focus on food applications. Studies on the degradation and the clearing of the hydrogels in medical applications focus on cell and drug delivery as on biocompatibility.\(^2,3\) These studies commonly include chemical degradation of hydrogels, mostly via acid–base hydrolysis.\(^4\) The gel structure loss is mostly via acid–base hydrolysis.\(^4\) The gel structure loss is driven by slow chemical processes and can be accelerated by pre-oxidation.\(^5\) Disintegration sometimes is also investigated in specific physiological fluids, for example, post oral hydrogel delivery.\(^6\) Several studies on photodegradable gels extend the possible gel degradation mechanism.\(^7,8\) Apart from photolabile gels, few studies aim at disintegrating gel matrices via external stimuli. Often disintegration of hydrogels is regarded as a material failure\(^9,10\) rather than a specific tunable property. Compressive disintegration of the hydrogel matrix is a mechanism for hydrogel degradation. This is of specific interest in vessels where the gels’ remnants would subsequently be washed out. The occlusion of the vasa deferentia (VD) in males is such an application, where hydrogel fragments would flow out from the vessel. Gels could serve as long-term male contraceptive in case gels prove stable in VD fluid. If the compressive disintegration proves feasible, the application is reversible upon external stimuli. The exposed location of the vas deferens in the scrotum of the male enable and facilitate compressive treatment of the vas deferens. The exposure of the vas deferens is exploited in vasectomy,\(^11\) and in the introduction of similar occlusive VD approaches.\(^12,13\) Though unimplemented, compression of the scrotal vas deferens is assumed viable.

The compression of the hydrogels is possible either by sophisticated compressive devices or by freehand compression by a nurse or physician. A sophisticated compressive device is less force-restricted, but one has to refrain from tissue damage. Both cases would probably elicit the use of analgesics. The force humans can apply to massage a vessel occlusion is limited. Average pinch forces of non-specifically trained hands are about 0.4 N mm\(^{-2}\).\(^14\)

Compressive disintegration of inlying gels is delicate as cells and tissues might also be affected by compression.\(^15\) Human tissues and cells, mostly due to the presence of collagen, exhibit shear stiffening behavior. This is important to prevent destructive tissue compression or -tension. Several hydrogels are also known to show shear stiffening behavior (e.g., ref. [16]). From the magnitude of tissue shear stiffening and hydrogel behavior, it can be concluded that hydrogels matrices at low biopolymer concentrations will break before tissue damage occurs.\(^17,18\) This can be a possible approach for the disintegration of hydrogels in tissue engineering. Compression of the hydrogels would result in loss of the matrix integrity and thereby the stabilizing or occluding effects while surrounding tissues would be mostly unaffected by compressive or massaging treatments. Selective

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application of extracorporeal shock waves on cells[19] and massaging for gel disintegration and ejection[22] apply this possibility.

We accordingly investigated the structural integrity and the breaking strain of hydrogels under compression. We did this in VD mimicking tube structures. We studied the compressive disintegration of κ-carrageenan (KC) physically cross-linked hydrogels. KC is known to form rigid and brittle hydrogels using monovalent cations, of which potassium ions are very efficient.[20] KC gel properties can be adjusted by, for example, biopolymer concentration,[21] degree of polymerization[22] as the addition of synergistic polymers.[23] Vas deferentia fluids are rich in potassium ions,[24] enabling stable KC physically cross-linked hydrogels. The immune modulation in the VD is expected to enable the hydrogel’s biocompatibility in vivo,[25] though commonly carrageenans are used in inflammation elicitation.[26] Additionally, a KC gel cannot be degraded by human enzymes, and it is assumed to reside long term in the VD. Random polymer scission can carefully be estimated by acid-base hydrolysis.[27] Exact ion and biopolymer concentrations were used. The concentration shifts can be used to adjust the gel structures to desired mechanical properties. Below we accordingly hypothesise that reversal of a hydrogel occlusion of the VD in the human male is possible by manual compression.

2. Experimental Section

2.1. Materials

Sodium chloride (NaCl), calcium chloride (CaCl₂) (Carl Roth GmbH & Co. KG, Karlsruhe, Germany), potassium chloride (KCl - Riedel-de Haën, Seelze, Germany now Honeywell) were all analytical grade. Food grade KC CW950 was received from Danisco S/A (Danisco SA, Copenhagen, Denmark). The used KC has a sulphate ester content of (24 ± 1) % and an inherent κ- and μ-carrageenan impurity of (10 ± 1) % and (3 ± 1) % respectively.[28]

Three different tubes (see Supporting Information) and a cut-down line (ZwickRoell GmbH & Co. KG, Ulm, Germany) were filled using a bottom clip. 3% by mass KC solutions could not be filled into tube A or B due to the viscosity and the rapid gelation of the solutions. The tubes were filled with a spatula and cut using the cuvette mould, before rheometric analysis.

1–3% by mass gels were chosen as the expected bulk modulus is sufficient to withstand the peristaltic compressions in the final application.

2.2. Gel Production

Dry KC was dissolved in deionized water, heated for 25 min to 80 °C, before compensation for evaporative losses and transfer into desired sample vessels. KCl and NaCl were added to obtain the desired potassium and 30 mM sodium concentration. Solutions of 300 mM potassium or 3% by mass were heated to 95 °C, 200 mM, or 2% by weight to 88 °C to ensure dissolution. Solutions were cooled to room temperature before compression or shear specification. 100 mM potassium samples of biopolymer concentration of 1–3% by mass were produced. 1% by mass samples of potassium concentration of 100–300 mM were produced.

Hot solutions were filled into one of the three tubes or the cuvettes. The tubes were preheated in an oven to 80 °C. This circumvents intra-tubal gel slippage due to cooling contraction of the gel matrix as ease of filling due to gelation retardation at the tube walls. The tubes were filled using a bottom clip. 3% by mass KC solutions could not be filled into tube A or B due to the viscosity and the rapid gelation of the solutions. The cuvette gels were extracted with a spatula and cut using the cuvette mould, before rheometric analysis.

2.3. Rheometry Measurements

Samples were clamped into a dynamic mechanical analysis (DMA) measuring system of a MCR302 rheometer (Anton Paar GmbH, Graz, Austria). Prior several measurements were run to determine adequate size and fixation of the gel matrices. Long gels eventually are expelled from the rheometer at high shear, while short gels suffered disproportionally from indentation of the metal jaw of the DMA system. Strong jaw fixation resulted in gel compression and a predetermined breaking point at the transition from jaw to gel matrix. Loose fixation results in erroneous data recordings. The 6 mm deep gels were compressed by the jaws to (5.65 ± 0.10) mm to assure firm but non-destructive fixation. (see Supporting Information) Fixation is a key limiting point of the method, but from comparison with gel compression data, we assume it a possible characterisation approach (vide infra).

2.4. Rubber Compression

Filled rubber tubes were radially compressed in a Zwick All-round Line (ZwickRoell GmbH & Co. KG, Ulm, Germany)
equipped with a 10 kN force cell. Two different compressive speeds were evaluated. We estimated the compression of a gel matrix in the VD (1 mm in diameter) by hand to last either 1 s or 3 s. The compressive speed was therefore set to either 1 or 0.3 mm s$^{-1}$. A minimum of three equivalent samples were tested. Data from individual runs were averaged. Since the load cell was partly used below its specified working range (<40 N) the response characteristics of the load cell were determined beforehand by calibration. The relevant force range of the load cell was specified via weight loadings. From calibration data by the manufacturer, we assume the response profile of tension cell was specified via weight loadings. From calibration data by the response characteristics of the load cell were determined beforehand by calibration.

3. Results and Discussion

3.1. Comparison of Tubes and Physiological Vessels

To determine if the tubes are possible vessel simulations, the compressive strength of empty tubes is compared with literature data from physiological systems. Compression data from the used tubes, porcine aortae (29) and model values for human aortae (15,30) are shown in Figure 1.

The tubes A–C used in the study show lower compressive moduli than the models for the human aorta. The closest approximation in the study are tubes A, also with respect to the porcine aorta data. Tubes A show an exponential increase in force for the initial deformation of the tubes. Once the compression exceeds the tube folding, the tube’s response increases super-exponentially. While tube A is closer to physiological values, the gel response is partly hidden by the tube’s compressive response. Therefore, tube B was added to the investigation.

The softer tubing more sensitively expresses the gels’ compressive responses. We found that the stiffness of the tubing is of super-exponential. While tube A is closer to physiological values, the gel response is partly hidden by the tube’s compressive response. Therefore, tube B was added to the investigation.

The softer tubing more sensitively expresses the gels’ compressive responses. We found that the stiffness of the tubing is of no impact on the gel disintegration. Since 3% by mass gels could not be filled into tube A or B, we also included tube C. Ultimately, for the gel properties chosen, vessels will always stiffen upon applied shear and gel structures break before vessel damage occurs (vide supra).

Little data on compression of vessels is reported, as vessels are usually loaded by intra-luminal pressure for which the tensile modulus is of interest. (10,31) Compressive vessel investigations found in literature focus on blood supply during pregnancy, cardiopulmonary resuscitation or aortae calcification determination. One study reported on calcified porcine aortae up to compressive strains of 50%, (29) strains too low for hydrogel disintegration. After 50% strain, the trend in compressive force is unknown. From comparison with the tube compression forces in Figure 1, we expect the force necessary to compress porcine aorta to increase more extensively after 50% strain. We accordingly use the aorta tensile modulus values, though the final goal is radial uniaxial compression, to estimate the upper limit of force required for vessel compression.

Upon compression, vessels deform and fold until the lumen vanishes. Due to the elastic lamellae, cells and collagen in aortae, as in the VD, we expect extensive compressive stress forces upon loading. The folding generates tensile stresses in the buckling zones due to collagen stretching. Vessel collagen is, besides its tensile stiffening effects, also known for its compressive stiffening properties. (15,32) It exerts comprehensive forces upon compression if collagen orientation is in compression direction. Furthermore, we assume the VD to behave similarly to compression as human aortae. The structures of the human aortae and the vas deferens are similar. (31,34) Aortae consist of elastic lamellae layers and smooth muscle cells in the tunica media, as an outer adventitial layer, circling a larger lumen. The energy stored in the elastic lamellae during systole forwards blood flow during diastole. The vas deferens has three smooth muscle sheets, two longitudinal and one circular, which drive vessel peristalsis. Though the general mechanism of action differs, the main constituents under compression in both cases are the smooth muscle cells and the adventitia. Aortae wall thickness was reported 1.53 ± 0.12 mm and 1.78 ± 0.15 mm for different age groups, (30) porcine aortae were 1.58 ± 0.30 mm thick. (29) Vas deferens wall thickness was reported 0.73 mm, with unknown standard deviation. (35) Thus, comparing a single aorta wall with a double-walled vas deferens renders a similar thickness of the structures. (18,35)

We want to emphasize that using human aortae data is a careful estimation of the compressive modulus, as the folding and deformation of the vessel lumen should result in significantly lower forces. Additionally, the forces for porcine aortae compression are also below these estimates. (29) Below, the modelled human aortae value was taken at 65% strain to compare gel-vessel compression with physical hand forces.

The use of tensile aortae stresses for VD compression stress suffers the following problems:

- compressive stress is assumed isotropic through different tensile moduli for axial and radial tensions are reported (38)
- we neglect the differences in histology of human abdominal aortae and VD
- stress–strain curves are exponential for aortae (Figure 1)
- calculation of the compressive modulus from the tensile modulus is only valid within the linear response of materials: \( E = 3K(1-2\nu) \), where \( E \) is the tensile modulus, \( K \) the compressive one and \( \nu \) the Poisson ratio
- assuming incompressibility, the bulk modulus is infinite

Figure 1. Stress–strain values for modelled human aortae (10) (solid line), porcine aortae (29) (dash-dot-dotted), tube A (dashed), tube B (dotted), and tube C (dotted-dashed).
the Poisson ratio was assumed 0.5, though it is usually undetermined for human aortae, as VD

One final comment is given concerning tube materials. We chose isotropic and homogeneous model tubes for the compressive investigation (to focus on the hydrogel properties, as restrict the number of necessary samples due to inhomogeneities), though these suffer direct compression resistive force matching with respect to human aortae models. Due to the possible additivity of the counter-compression force contributions, this should not obscure the conclusions drawn. To our understanding, the choice of the model does not diminish the validity of the approach.

3.2. Tube-Gel Compression

1% by weight and 100 mM potassium KC gel-filled rubber tubes compression data is shown in Figure 2a. This data includes the tubes’ compression responses. In Figure 2b we subtracted the tubes’ stresses from the data. We find that due to the lack of interaction, the tube’s response can be added to the gel response and vice versa.

There is a clear gel response behavior for tubes B and C visible in between 40% to 70% shear from an actual decline of the force curves (Figure 2a). This decline is partly absent in tube A. Therefore, the specific gel breakage expected at around 60% shear for these more rigid tubes, is not perceived. It is perceivable if the tube stress is subtracted (Figure 2b). There is a stress and a strain shift in the peak force for tubes C. Both are related to geometrical issues. Stress increases as the surface area of compression on the gel increases. Strain shifts derive from diminished gel supporting effects by the tubes, resulting in earlier wall detachment and lower strain ruptures. Below, we accordingly compare DMA rheometry data with the less supported gels in tubes C.

Several minor peaks in Figure 2b are present, which derive from prior differences in tube diameters. These go against clean averaging of the different samples. There is relatively little difference in force required for peak values around 60% shear for tubes A and B. As there is also no obvious single peak visible in the data, the question of the strain at gel breakage remains unanswered. Especially accounting for an unspecified, partial compression of the tube walls. Different tubes should show slightly different breaking strains, due to rigidity properties. These are however concealed due to the sensitivity of the experiment and the minor differences in initial tube diameter. To further elucidate compression on gels we extended the samples to different potassium concentrations and biopolymer concentrations.

These influences are visualized in Figure 3a,b, the former showing gels of different potassium concentrations in tube B, the latter different biopolymer concentrations in tubes C. From Figure 3a a double or triple peak structure for different potassium concentrations is obvious. By visual observation of samples during compression, two or three stages can be differentiated. First, parts of the compressed gel matrix detach from the wall of the tubes, as the tubes expand transversal to the compression direction. Two effects drive this phenomenon. First, the difference in Poisson ratios of the two materials results in differences in lateral expansion. Poisson ratios of 0.5 have been proposed for KC/locust bean gum gels, but we assume pure KC gels to have a lower Poisson ratio, at least lower than the tubes. Second, since the volume inside the tube decreases, for volume constancy the “incompressible” gel is squeezed out of the tube on both sides. This results in tube-axial expansion of the gel network and possibly necking, which results in wall detachment. Which of the two effects dominates cannot be concluded. Upon further compression, the gel matrix breaks down at a single or several spots. This is driven by both, the uniaxial compression as the tube-axial extension. From the assumption of similar behavior in compression and tension, the diameter compression of the gel for various Poisson ratios can be calculated, at which extension results in rupture. For a Poisson ratio of 0.5, this would theoretically be 4.47 mm of 6 mm (see Supporting Information).

There is a force depression in the measurement upon gel wall detachment, probably due to a loss of rubber tube stabilisation. The multiple initial ruptures and crack propagations

Figure 2. Stress recorded from gel-filled tube compression for tube A (dashed), tube B (dotted), and tube C (dot-dashed) with a 1% by mass KC gels with 100 mM potassium. a)Recorded stress for tube-gel response. b) Recorded stress with tube response subtracted.
then drive a chaotic formation of peak force during breaking. If gels only break at one specific position, as in the case of the 300 mM or 3% by mass gels, the multiple peaks are replaced by a relatively clean double peak. The detachment of the tube wall as the shear break happens earlier for 200 and 300 mM gels as these have lower Poisson ratios than the 100 mM gel. The former gels are less flexible. The required breaking force also depletes, which is in accordance with Dunstan et al.\[17\] This depletion might also partly be affected by the fast cooling rate, which hinders clean micro- and macrostructure build-up.\[38\]

To compare with freehand compressions of the gels we conducted several measurements using an increased compression speed. A direct comparison of the two different compression speeds on the gel response (Figure 4) indicates that there is no increase in the recorded stresses of the gel matrices. The viscoelastic gel does not behave markedly altered at the given strain speeds of 1 and 0.3 mm s\(^{-1}\). We assume that the tubes' compression stress also do not alter significantly with speed. Both stress changes would affect the force data. Accordingly, little differences in gel stress for manual compression will be present for different compression speeds. It is literally the medical personnel's decision to choose hand compression speed. We note that disintegration peaks are shifted to lower strain values, as gel structures are given less time to adapt to the compression. Crack propagation happens at lower strains. Lower strains are of advantage, as this also decreases the vessel compression stress simultaneously, decreasing the required total disintegration force.

### 3.3. Optical Gel Compression Observation

To optically allocate the peaks to the processes in the gel matrix, we used tube A gel samples that were strained to a maximum of a) 50%, b) 65%, and c) 75%. The respective post-compression removed tube gels are pictured in Figure 5a–c.

In these part-compressions, the behavior of the gel matrix in the rubber tubes is clearly seen. The 50% strain sample shows gel squashing. Due to the fluidic nature of the gels, it stays compressed after tube withdrawal. Compressing a gel to 65% results in several cracks in the gel matrix. Straining the sample even further or pausing at 65% strain, these cracks propagate leaving multiple gel parts. The multiple cracks of the gel are probably due to the plan-parallel alignment of the compression. Upon finger compression, there is only a single rupture of the gel matrix to be expected. A nurse or physician would have to compress multiple times, eventually massaging, to ensure complete disintegration of the gel matrix.

### 3.4. Rheometry Gel Rupture Investigation

To cross-validate gel-breaking strain, we used a rheometer with a DMA measuring unit. The shear dependent storage moduli of the gel matrices are pictured in Figure 6.
These gels undergo increasing strain at 1 Hz oscillations. The gel matrix does not fully recover during this short time period, resulting in initial decreases of the storage moduli of the gels. This is most prominent in the initial 3% by wt. sample storage modulus decrease. The fixture of the gels consists of solid metal edges, which do indent the gel matrix irreversibly during measurement. With increasing shear, the gel block eventually starts ripping until the crack propagates throughout the matrix. This results in the marked decay of the storage modulus between 40% and 65% shear. These torsional breaking values are compared with the values obtained from the compression measurements (Table 2).

We defined a gel in the DMA to be broken once it decreased to 30% of its initial storage modulus. For lower thresholds values a complete rupture of the gel matrix is present but this is a shift to higher shear values of breaking. Higher reported values are above the initial breaking shear and do not represent the desired values. Using higher thresholds is problematic as the storage modulus depression from restructuring upon shear oscillations does neither represent gel rupture.

Whey and muscle protein gels show little differences in shear stress and strain compared to torsion stress and strain.\(^{[37]}\) We expect for our homogenous, isotropic gels an equivalent behavior. Fracture planes of samples showing angles to the perpendicular plane of the rheometer axis imply that the sample fails not solely from shear, but partly from compression.\(^{[37]}\) Samples of 1% and 2% by mass had non-perpendicular fracture planes, while 3% by mass were perpendicular, indicating the shear break character of the 3% sample. 1% by mass gel samples show a higher spread in the samples’ breaking storage moduli. These gels were substantially affected by the metal edge indentation of the DMA jaws.

We also compared DMA gels with data from gel disks breaking in a serrated plate (PP) measuring unit (50 mm diameter, \(F_n < 0.5 \text{ N}\)). Unluckily, this comparison is of no information due to the different modes of breaking. The DMA gels withstand shear until an initial crack in the gel block appears which propagates throughout. In the PP unit, gel matrices break progressively below the serration pins, at the outer radius first, slowly moving inward with increasing shear. (see Supporting Information)

The standard deviation of the compression data (Table 2–graph shading) is an approximation to the chaotic and parallel crack propagation in the gel. It also partly includes the force necessary for slow squeezing out the gels of the tubes. Giving more time for crack propagation and gel relaxation by slow compression would probably narrow the underlying fitted Lorentzian model and thereby the reported error. (see Supporting Information)

### 3.5. Compression and Hand Force Comparison

At the obtained breaking strains, we can compare the force values for gel disintegration inside a tube/vessel with the physical hand force. We used a strain of 65% in the following estimations. Several factors are accounted for. The physiological vessel shows a 2–3 times higher compression modulus at 65% strain compared to tubes A. We, therefore, calculated the force values based on the modelled aortae data. The compression data was derived from estimated 60 mm × 8.775 mm areas for the gel sample surface at fracture (see Supporting Information). Required disintegration pressures are sums of the pressures for gel disintegration and vessel deformation. Since 3% by weight gels could only be prepared in tubes C, we used this respective

| KC gel [% by wt.] | 1     | 2     | 3     |
|------------------|-------|-------|-------|
| DMA              | 41.3 ± 8.7 | 51.5 ± 8.0 | 61.4 ± 7.8 |
| Compression      | 54.0 ± 5.6 | 57.8 ± 7.7 | 57.3 ± 12.7 |

Figure 5. Tube A extraction 1% by mass 100 mM potassium KC gel images after compression to 50% (left), 65% (middle), and 75% (right) strain.

Figure 6. Storage moduli development during amplitude sweeps at 1 Hz for 1% (dotted), 2% (dashed), and 3% (dotted-dashed) by mass 100 mM potassium KC gels. Blue coloured shadings are standard deviations of the averaged data.

Table 2. Comparison of breaking strains from compression and torsional shear in % of strain.
gel break estimate for the 3% by mass gel. For 1% and 2% gels we used gel break estimates from tube A.

Respective finger forces, of lateral and palmar pinch, are reported to be roughly 0.40 and 0.24 N mm$^{-2}$ respectively. These values are compared with the obtained compressive forces (Table 3). These values should only be regarded as approximations due to the underlying assumptions. The values for compressive porcine aortae data are listed for comparison reasons but are not considered in the following.

Possibly the 1% by mass gel can be disintegrated by lateral pinching and massaging of a KC gel inside the VD. At least theoretically from physicians generating pinch forces above the reported mean values. The underlying strength data has a standard deviation of close to 40%, so individual pinch strength likely differs considerably between physicians. 2% and 3% by mass gels will not be disintegrable manually, at least by the majority of masseurs. For further consideration, we note that VD plugs are estimated to have 10 mm $\times$ 1 mm size, which reduces the force required for disintegration. In any case, the necessity of some kind of compressive device is present, be it only to focus hand forces. This triggers further medical concerns to ensure avoidance of tissue damages.

### Table 3. Pressures required for gel disintegration following a radially compressed model vessel$^{[29]}$.

| KC gel concentration [% by wt.] | 1      | 2      | 3      |
|--------------------------------|--------|--------|--------|
| Tensile human aortae [N mm$^{-2}$]$^{[30]}$ | 0.45   | 0.55   | 0.70$^a$ |
| Compressive porcine aortae [N mm$^{-2}$]$^{[29]}$ | 0.20   | 0.30   | 0.46   |

$^a$An increased gel compression area (15 mm $\times$ 60 mm) with less gel-tube stabilisation makes it difficult to compare with 1% and 2% by mass gels. We used the recorded force with the small compressive surface area to obtain the value, which is formally incorrect (see Supporting Information).

4. Conclusion

Upon compression, mainly the stress of the physical vessels determines the force required for the compressive disintegration of the gel matrix inside ($F_{\text{vessel}} \gg F_{\text{gel}}$). The gel only has a minor effect on required compressive forces. The tube model for gel disintegration was successfully used to specify the hydrogel breaking strain, as to perceive the breaking mechanism, and specify that disintegration force contributions can be handled cumulatively. The studies showed that physically cross-linked KC gels of 1–3% by mass biopolymer concentration break below 70% strain. For the understanding of the gel-tube system, it is useful to use softer and stiffer tubes. While the stiffer tubes more closely resemble the tensile and compressive properties of physical vessels, the softer tubes show the hydrogel response more prominent. From aortae models, the forces required for intra-vessel gel disintegration can be estimated. We used the aortae model since we assume similarity to the VD. We intentionally decided to use the upper force estimate of tensile human aortae loading. This intention bases on the unknown trend of compressive forces in porcine aorta compression above 50% strain, and in prudence to differences in applicants VD thicknesses and structures,$^{[35]}$ which alter the required forces. Summarising we find manually applied pinch forces to be insufficient to disintegrate gel matrices in modelled vessels. It is unlikely that nurses or physicians will be able to disintegrate VD occluding gels by hand. We accordingly reject the study hypothesis. Preventing or minimizing tissue damage, sophisticated compressive devices (e.g., adapted roller presses) or specific forceps, which prevent hydrogel pre-compression dislocation, might be usable for the hydrogel disintegration to overcome the human force deficiency. The use of rigid hydrogel fillers, for example, microspheres, would render composite structures disintegratable via extracorporeal shock waves. Light-sensitive hydrogel cross-linker, or secondary medical procedures are unfavourable.

Besides the used methods, the study could be enhanced by the following approaches. The DMA rheometry study could be enhanced by smaller steps of shear increase. We tried to include edge protection in the DMA for the gel matrix without success. Probably rounded metal clamps parts would slightly ameliorate gels’ DMA data. Samples could also be capstan shaped to obtain true fracture at the geometric indentation. Compression speeds could be diminished for the breaking response in the signal to be sharper. The tube compression study does not include wall friction influences, or tube compression, that might affect the gel-tube system. We assume this does alter the compressive forces needed for the disintegration of the gels only a little.

Besides measurement improvements, the study is to be extended on medical issues. One major medical concern of occluding the VD is the appearance of secondary obstructions.$^{[39]}$ Secondary obstructions are highly critical, as these cannot be resolved by massage or compression. Nevertheless, using a hydrogel is one possible method to possibly circumvent obstructions, as fluid passage is present. Avoiding secondary obstructions is of primary interest for the application. Furthermore, the influence of cells and proteins on gels is of irrefutable interest for the application.

### Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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### Conflict of Interest

The authors declare no conflict of interest.

### Keywords

biomedical, compression, contraception, hydrogel, $\kappa$-carrageenan
