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Comparative *in vitro* evaluation of microspherical embolisation agents

Andrew L. Lewis · Clementine Adams · Wendy Busby · Stephen A. Jones · Laura C. Wolfenden · Simon W. Leppard · Rosemary R. Palmer · Sharon Small

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Abstract This study describes the comparative performance of four commercially available microspherical embolisation products: Embosphere™, Embogold™, Contour SE™ and Bead Block™. A series of *in vitro* evaluations were designed to assess the mechanical and biological characteristics of these biomaterials. Size distribution analysis revealed sieving techniques used to fractionate the embolics produced similar size distributions. The forces required to compress Embosphere, Embogold and Bead Block were in the range 21–27.5 kPa. Contour SE was significantly more compressible at ∼5 kPa. However, recoverability of Contour SE required several minutes in contrast to the other products, a phenomenon attributed to its macroporous structure. When time taken to reach and remain in suspension was studied, results showed that the products quickly reached equilibrium with contrast agent. Bead Block was maintained in suspension for twice as long as the other products. Catheter deliverability was assessed and found to be dependent upon both microsphere and catheter, the best combination being Bead Block delivered via the Progreat™ catheter. Both the blood contacting SEM and plasma coagulation time showed none of the products were pro-thrombic or pro-coagulatory, each producing comparable results. Small differences in physical properties such as compressibility, could play an important role in delivery and effectiveness of vessel blockage. Currently all products are used routinely in clinical practice.

A. L. Lewis (✉) · C. Adams · W. Busby · S. A. Jones · L. C. Wolfenden · S. W. Leppard · R. R. Palmer · S. Small
Biocompatibles UK Ltd, Farnham Business Park, Weydon Lane, Farnham, Surrey, GU9 8QL, UK
e-mail: andrew.lewis@biocompatibles.com

1 Introduction

Embolisation therapy is a growing area of minimally invasive surgery performed by the interventional radiologist (IR). For many years, these physicians have been treating a variety of conditions by entering the vasculature via a minor incision, usually in an artery of the arm or leg, and gaining access to the treatment site by use of guidewires and catheters aided by imaging techniques such as fluoroscopy. Once at the site the radiologist employs one of many devices or agents that bring about embolisation and thus blockage of the vessel. This might be in order to treat a hypervascular tumour, such as malignant hepatocellular carcinoma of the liver [1], or benign uterine lyomyomata or fibroids [2]. In these cases, the blockage of the artery serves to cut off the blood supply feeding the tumour and thus bring about its necrosis and shrinkage. The treatment site may alternatively be an arteriovenous malformation (AVM), essentially an abnormal connection between artery and vein which is commonly treated by closure using embolisation [3].

When blocking an artery, the IR has a choice of devices dependent upon the desired end result. Large arteries can be blocked by application of thrombus-promoting shape-memory coils that unravel in the vessel, or detachable balloon assemblies. Cyanoacrylate glues find favour with only those most experienced IRs owing to the potential complications of glueing the catheter to the patient. Biodegradable materials are sometimes selected where an IR has a desire to reintervene in the same artery at a later date. Autologous blood clot has been used [4, 5], but Gelfoam™ gelatin slurry is the most commonly used agent where biodegradability is required in order to re-enter a vessel at a later date [6]. Polyvinyl alcohol (PVA) sponge particles are one of the most generally used permanent embolic agents for a wide variety of treatments, and have been used successfully since the mid 1970s [7, 8].

The irregular shape of the PVA causes the particles to aggregate and block quite proximally in the vessel once released from the catheter. The development of microcatheters over recent years has enabled the IR to perform increasingly superselective embolisation in which the catheter is placed as close to the treatment site as possible. These catheters possess extremely narrow inner lumen diameters, and a consequence of this is that PVA particles tend to aggregate and block the catheter. This has spawned a new generation of compressible spherical embolisation microspheres that are designed to deform during delivery through the catheter, overcoming the blocking issue, and then to be carried by the blood flow to the point where the size of the microsphere determines the point of blockage (rather than a more proximal and less predictable embolisation caused by particle aggregation). In this way the IR can select the size range of the embolic agent according to the size of the vessel at the point of treatment [9].

The first commercial spherical embolisation agent available for use was Embosphere™, a collagen-coated microsphere with a trisacryl core commercialised by Biosphere Medical [10]. This was supplemented by Biosphere Medical with Embogold™, essentially the same product treated with a gold colloid to generate a red colouration to help the IR visualise the product more effectively in the syringe used for delivery. More recently, two additional microsphere products have been made available to the IR; Contour SE™ is a microsphere based on PVA from Boston Scientific which complements its Contour™ range of PVA particles. Bead Block™ is also a PVA-based microsphere product from Biocompatibles UK Ltd and is based on *N*-fil Technology™ originally developed as a contact lens material. These PVA beads are tinted blue using contact-lens technology in order to improve their visibility and handling in clinical use. The purpose of this paper is to describe the comparative performance of these four microsphere products in a selection of *in vitro* evaluations designed to assess the mechanical and biological characteristics of these biomaterials.

2 Materials and methods

2.1 Materials

The microspheres under evaluation were Bead Block™ (Biocompatibles UK Ltd, UK), Contour SE (Boston Scientific Inc., USA) and Embosphere/Embogold (Biosphere Medical Inc, USA). The catheters used for assessment of deliverability were the Progreat 2.8/3.0 Fr microcatheter Omega (Terumo, Japan), the Renegade Hi-Flo 2.8/3.0 Fr microcatheter (Boston Scientific Inc., USA) and the Embocath 2.8/3.0 Fr microcatheter (Biosphere Medical Inc., USA). Isovue 300 contrast medium (Bracco Diagnostics Inc., USA) was used in the deliverability tests and to form the suspensions of the microspheres.

2.2 Size distribution

Size distributions were determined using images of 700–900 μm and 900–1200 μm microspheres photographed using a CCD camera and microscope then the diameters resolved with Image Pro Plus 4.05. Microspheres in 1–2 ml of saline were transferred to small cell culture flasks; between 50 and 1500 beads were photographed per image. Image Pro Plus 4.05 resolved the diameters of between 100 and 1500 microspheres dependent on size range. Diameters were tabulated and converted to histograms of size range versus frequency, normalised and represented as graphs using Microsoft Excel.

2.3 Compression testing

The force required to compress the embolic materials over a fixed distance was evaluated using a compression test. A flat 5 mm diameter cylindrical probe was attached to an Instron Material Testing Systems Model 4411 (Instron, High Wycombe, UK) mounted with a 50N load cell. A close packed monolayer of test sample, 700–900 μm size range, was placed on the sample pan, underneath the probe, to cover an area greater than the size of the probe. Excess water was removed from the sample by wicking with tissue. The probe was positioned just above the sample using a specimen gauge length of 1.0 mm and the load balance zeroed. The probe was then extended by 0.85 mm using a crosshead speed of 5.0 mm/min and the load data recorded. From the data the maximum compression force was calculated at 8–16% compression strain. Each measurement was performed five times per sample and the mean, standard deviation and coefficient of variation calculated.

2.4 Microsphere suspension evaluation

For these studies only one size of microsphere was assessed (500–700 μm range) for comparative purposes. It should be noted that microsphere size and contrast agent type will have a large influence over the suspension properties of the products.

2.4.1 Time taken to achieve suspension

Contour SE microspheres were transferred from the vials in which they were supplied into 20 ml syringes comparable with those containing Bead Block and Embosphere. Embogold was not evaluated in this experiment. 5 ml of Isovue 300 were drawn into a 5 ml syringe. This volume is equivalent to the total volume of embolic agent in buffer supplied for each product and is the volume recommended in each product's Directions for Use. This was added to each 20 ml syringe of embolic agent by means of a 3-way connector, and timing was started. Air was expelled from the syringe, which was

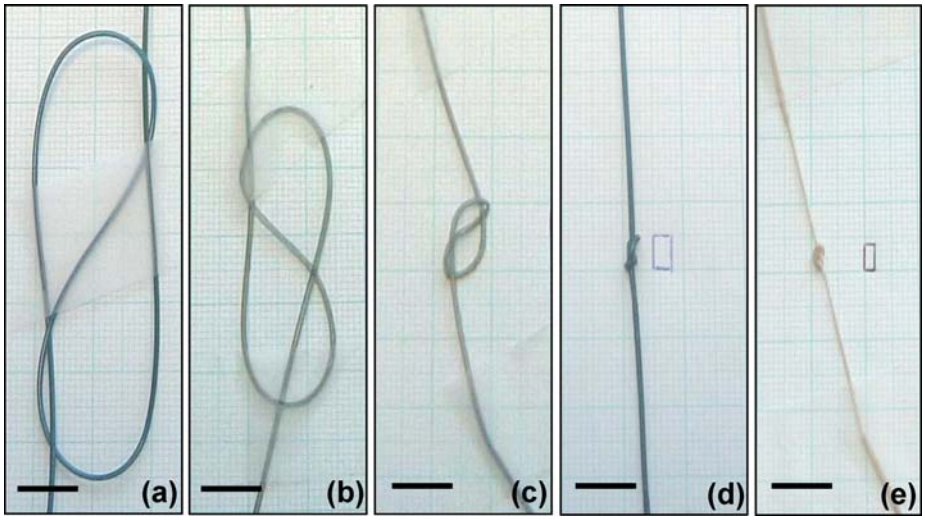

Fig. 1 "Figure 8" tortuosity loops used to assess catheter deliverability (a) 6.5 × 2 cm; (b) 4.5 × 1.5 cm; (c) 1.5 × 0.8 cm; (d) 0.5 × 0.3 cm; (e) 0.4 × 0.2 cm (scale bar = 1 cm)

sealed, inverted gently several times and then inspected. If a suspension had not formed, the inversions of the syringe and inspection were repeated, until a stable suspension of microspheres was observed, lasting for >1 min. The time taken for this suspension to form was recorded. Two replicates of each product were tested, with the exception of Bead Block, which was tested three times.

2.4.2 Time maintaining suspension

Contour SE were transferred from their vials into 20 ml syringes as described above. 5 ml of Isovue 300 was added to each 20 ml syringe of embolic agent as described above. Air was expelled from the syringe and the syringe was sealed and inverted gently several times and then inspected. If a suspension had not formed, the inversions of the syringe and inspection were repeated, until a suspension was observed. Timing was started and the syringe was left to stand until the suspension was lost. The time taken for the suspension to remain was recorded. Suspension was taken as remaining while at least 2/3 of the volume of the syringe contained embolic product. The syringe was then inverted again 2–3 times and timing re-started, with the syringe left standing as before. Once again the time taken for the suspension to remain was recorded. If the first suspension remained for longer than the second, the experiment ceased, and the first suspension was taken as the maximum time in suspension. If the second suspension remained for longer than the first, re-suspension and settling was repeated until the time in suspension began to decrease. The longest time in suspension was then noted. Five replicates of each product were tested using the same method.

2.5 Catheter deliverability

To perform the catheter deliverability test Bead Block, Contour SE and Embosphere (500–700 μm or 700–900 μm size ranges) were mixed with saline (0.9 wt% NaCl in distilled water) and Isovue 300 contrast medium to form a test solution using two 3 ml plastic syringes (Becton Dickinson Medical, USA) and a 3-way connector (Becton Dickinson Medical).

The catheter under assessment was coiled into a 'Fig. 8' loop in order to emulate tortuosity encountered when used in clinical practice. An increased tortuosity was represented by increased tightness of the loop as shown in Fig. 1(a)–(e). These loops were measured in order that they could be reproduced reliably for each test.

When an even distribution of the spheres was obtained post mixing, the desired catheter was attached to the third port of the three-way stop-cock. The product was delivered through the desired catheter by drawing 1 ml of suspended microspheres into the syringe that was in-line with the catheter and slowly injecting the total contents. Once delivered, a further 1 ml was drawn into the syringe and the procedure repeated. The process was repeated for the final 1 ml aliquot if the catheter had not been completely blocked. Both the ease of delivery and extent of clogging were scored according to a predetermined scoring method (Table 1). If no clogging occurred the score was 0; if the catheter clogged once during

Table 1 Scoring for catheter deliverability studies

Score	Bead aggregation	Catheter clogging	Ease of injection
0	No	None	Easy
1	Yes	Once	Somewhat difficult
2	N/A	Twice or more	Difficult

the delivery of the 3 × 1 ml volumes the score was 1; if the catheter clogged twice or more during the delivery of the 3 × ml, then the score was 2. Each assessment was repeated three times for the larger loop sizes (Fig. 1(a) and (b)) and five times for the smaller sizes (Fig. 1(c)–(e)).

2.6 Blood contacting and scanning electron microscopy inspection

Known weights of Bead Block, Contour SE and Embosphere (target weight 0.3 g) were placed in duplicate polystyrene test tubes (Sarstedt, Leicester, UK), and 4 ml of citrated blood, (collected not more than 2 h earlier in monovettes containing tri-sodium citrate (Sarstedt)), were added to each. Additional samples of each microsphere product were placed in test tubes with 4 ml phosphate buffered saline (PBS, Inverclyde Biologicals, Strathclyde, UK) as controls. The test tubes were capped and placed on a roller mixer for 1.5 h at room temperature. After this time, the blood in each tube was carefully pipetted off using a glass Pasteur pipette, and the spheres were washed with PBS. The washing procedure involved adding 4 ml of PBS to each tube, agitating the contents gently and then pipetting off the liquid. This was repeated to give 4 rinses in total. 4 ml of 2% glutaraldehyde (Sigma, Poole, UK) in PBS were added to each tube and the tubes were capped with clean caps and placed on a roller mixer for 10–15 min at 20°C. The microspheres were then washed in PBS following the procedure described above, and finally in water using the same method. The microspheres from each vial were transferred onto carbon adhesive discs mounted on SEM stubs (Agar Scientific, Stansted Mountfitchet, Essex, UK) and these were placed in a dessicator overnight. SEM inspection of the dehydrated microspheres was carried out using a Hitachi S-3500N Scanning Electron Microscope.

2.7 Plasma coagulation time

Known weights of Bead Block, Contour SE and Embosphere (target weight 0.2 g) were placed in glass test tubes and 4 ml of defrosted fresh frozen plasma (which had been anticoagulated with tri-sodium citrate (National Blood Service, Bristol, UK)) were added to each. The tubes were sealed with Parafilm and inverted several times to ensure complete exposure of the microspheres to the plasma. 4 ml of plasma was also placed in an empty glass tube and treated in the same manner as a control. All the tubes were placed in a water bath at 37°C for 1 h. They were then immediately placed in an ice bath to retard any further activity of the proteins involved in the coagulation process. The plasma was removed from each of the test tubes using glass Pasteur pipettes, leaving the microspheres behind (where these were present), and transferred to clean glass tubes. These tubes were maintained in the ice bath until analysed. Measurement of the plasma coagulation times was carried out by removing five 500 μl aliquots from each of the tubes of chilled plasma into clean glass tubes which were then incubated in a water bath at 37°C for 5 min. After this time 500 μl of 0.02 M calcium chloride (Sigma) solution in distilled water, pre-warmed to 37°C, was added to each tube and timing was started. The time taken for a fibrin clot to become visible in a test tube was recorded as the coagulation time.

3 Results

3.1 Physical properties

3.1.1 Visual assessment

Figure 2 shows photographs of Bead Block, Contour SE and Embosphere (size range 500–700 μm) taken under a light microscope. Bead Block (Fig. 2(a)) is easily visualised due to the blue dye that tints the microsphere. The product appears very spherical and consistent in shape. Contour SE (Fig. 2(b)) produces a much darker image as the light cannot penetrate easily through the product. Some aggregates were visible (centre) and small "shark-fin" protrusions were evident on the outside of the microspheres that were generally elongated in shape. Embosphere were much more difficult to visualise due to their translucent nature (Fig. 2(c)). The product was generally spherical but there were occasional spheres trapped within a capsule (centre).

3.1.2 Size distribution

Whilst the majority of the microspheres were within the quoted size range, there were microspheres found outside of these limits (Fig. 3(a) and (b)). In particular, for the size range 700–900 μm, all the products tested had significant numbers of microspheres below the 700 μm lower limit. For all products in this size range the mean microsphere sizes were within a 50 μm range of each other and the difference between smallest and largest microspheres was ∼250 μm. For the 900–1200 μm size range for all products the mean sizes were within a 100 μm range of each other with the difference between smallest and largest being ∼250 μm for Bead Block and Contour SE, and ∼300 μm for Embosphere and Embogold. Whilst the size distribution was relatively "normal" for the 700–900 μm range, the 900–1200 μm distribution appeared more skewed for all products.

3.1.3 Compressibility

Figure 4 shows the force (kPa) required to compress the microsphere products in the size range 700–900 μm. This is the maximum size recommended for use with a microcatheter.

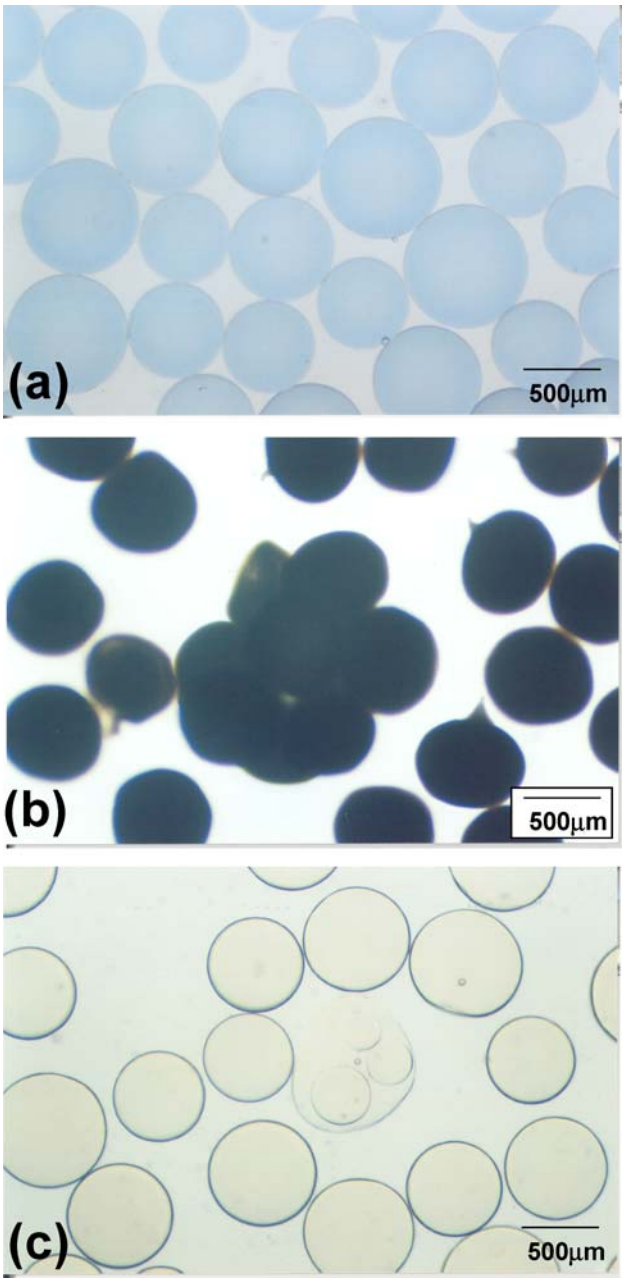

Fig. 2 Microscope pictures of (a) Bead Block; (b) Contour SE and (c) Embosphere (scale bar = 500 μm)

Data from the size ranges smaller than 700 μm have not been shown since using the test method employed, these sizes produced too high a degree of variation for the results to be meaningful. The Embosphere, Embogold and Bead Block microspheres were shown to have comparable compressibilities in the range 21–27.5 kPa. The force required to compress Contour SE was substantially lower than the other products, with a mean compression force of less than 5 kPa. This indicates that this product is far more easily compressed then the other microspheres. Further, if each of the products is squeezed lightly between the fingers, whilst Bead Block, Embosphere and Embogold possess some resilience to the applied force, the Contour SE microspheres will collapse flat and will not recover their shape for several minutes. This points to an inherent difference in the structures of the microspheres.

3.1.4 Suspension studies

Embolic microspheres are introduced into the desired blood vessel via a catheter and mixed in suspension with a suitable radiopaque contrast imaging agent. A homogeneous mixture with the contrast agent aids in the delivery of the microspheres by reducing the tendency for aggregation and hence blockage of the catheter. Moreover, the radiopaque nature of the contrast agent allows the IR to see where the embolic product is going and determine when the blood flow has been successfully arrested. A suspension study was performed on the commercial microsphere products using a typical non-ionic contrast agent, Isovue 300. Figure 5(a) demonstrates that all products require a short time to equilibrate to the saline:contrast mixture in which they are suspended prior to injection down the catheter. Of the products tested Contour SE reached isobouyancy (a homogeneous suspension suitable for delivery) the most quickly in just over 2 min. Embosphere took 3 min and Bead Block just over 4 min. Having obtained an isobouyant suspension, an important factor is the length of time for which the microspheres will remain in suspension before settling out and requiring re-suspension. The Bead Block microspheres remained suspended for over twice as long (>4.5 mins) as the Contour SE and Embosphere products (Fig. 5(b)).

3.1.5 Catheter deliverability

Catheter deliverability is a key performance characteristic of an embolic microsphere. The move away from irregular PVA particles has been primarily driven by the improvements in deliverability provided by the spherical products (i.e. reduced catheter blockage). Figure 6(a) and (b) show the degree of catheter clogging experienced for 500–700 μm and 700–900 μm microspheres of the various embolic agents with the matched catheter with which they are normally sold. When delivered through catheters with increasing levels of tortuosity, increased levels of catheter blockage are experienced. These data clearly show that there is an advantage to the combination of Bead Block through a Progreat catheter compared to the other product combinations. Degree of clogging increases in the order Bead Block/Progreat < Contour SE/Renegade ≪ Embosphere/Embocath. As expected, blockage is more frequent and occurs at lower tortuosity, when the microsphere size range is larger.

The evaluation was repeated in a study in which a single catheter type, Renegade, was used. Figure 7 shows that the same trend is observed with respect to microsphere size.

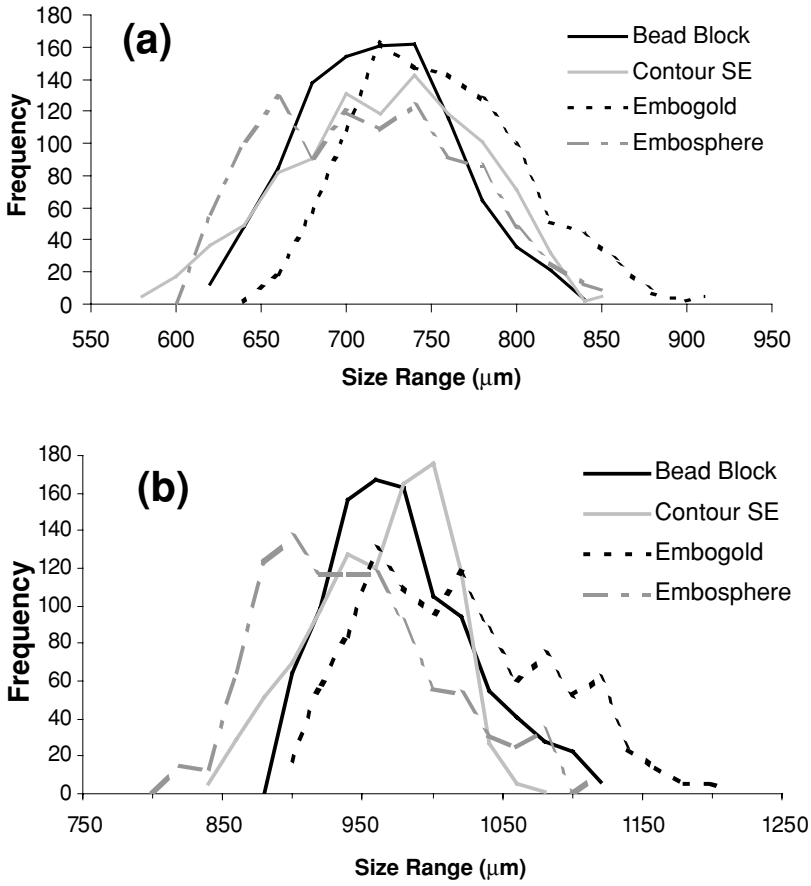

Fig. 3 Size distribution of commercial embolisation microspheres for the (a) 700–900 μm range and (b) 900–1200 μm range

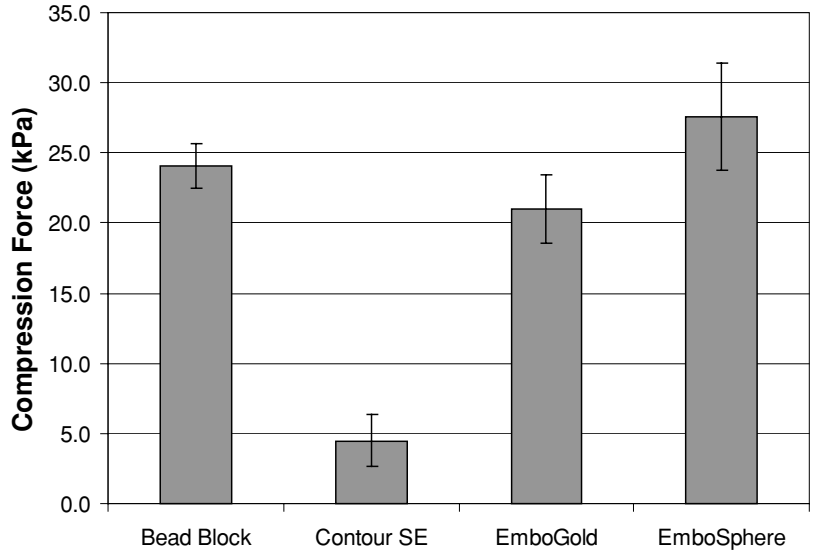

Fig. 4 Comparison of the compressibility for embolisation microspheres

Embosphere however, does not perform as badly as in the previous study where it was matched with Embocath. For the 500–700 μm size, there is no observed difference between the products, although there is a trend suggesting Bead Block < Embosphere < Contour SE for degree of clogging. For the 700–900 μm size range the result is more clear with degree of clogging increasing in the order Bead Block < Embosphere $\ll$ Contour SE.

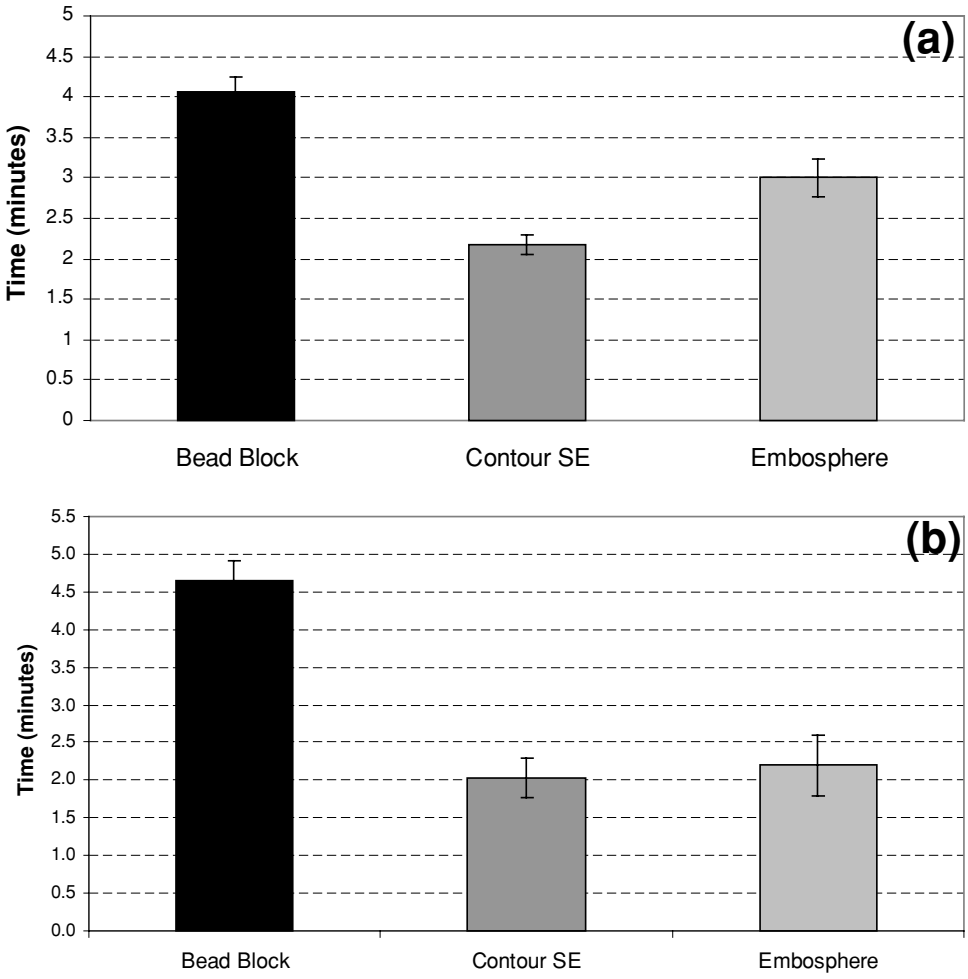

Fig. 5 Time taken to (a) reach suspension and (b) remain in suspension, after mixing with contrast agent

3.2 Biological properties

3.2.1 Blood contact SEM study

Each of the commercially-available microsphere products was subjected to blood contacting and SEM inspection in order to evaluate the interaction of the materials with blood components. Figure 8 shows a selection of representative micrographs for each product. Figures 8(a)–(c) show the Bead Block microspheres; Fig. 8(a) are microspheres that have not been blood-contacted, whereas (b) and (c) are post blood-contacting at two different magnifications. The SEM images clearly show the sphericity and uniformity of size for the Bead Block product; there is however, very little evidence of any thrombus formation, platelet or other cellular adhesion to this material. Figures 8(d)–(f) show Contour SE where Fig. 8(d) is pre blood-contact and (e and f) are post blood-contact at two different magnifications. In this case the microspheres have lost their spherical shape during the processing and imaging in high vacuum. Figure 8(f) shows a microsphere that has been torn apart as the material has collapsed to reveal a highly porous internal structure. Once again, the blood contacting micrographs show little evidence of blood component adhesion to the material. Figures 8(g)–(i) and 8(j)–(l) show micrographs for Embogold and Embosphere microspheres respectively. These are essentially the same materials except that Embogold has a gold colloid included within its structure to provide the microsphere with a red tint and improve its visibility by eye over the almost transparent Embosphere. Figures 8(g) and (j) are the pre-blood contact micrographs and Figs. (h) and (i) and (k) and (l) show the post-blood contact for the two products. Although these products are spherical microspheres, there are holes and dimples within the surface of the spheres. There is also evidence of smaller spheres and particulates. This may be due to defects in the collagen coating that is applied to the outside of these microspheres. Blood contacting again shows no evidence of thrombus or cell adhesion to these materials. Higher magnification of the post blood-contacted products show small crenulation of the surface. It is believed that this roughening of the surface has been caused by the effect of the blood on the collagen coating, although this has not resulted in any increase in the adhesion of cellular or proteinaceous materials.

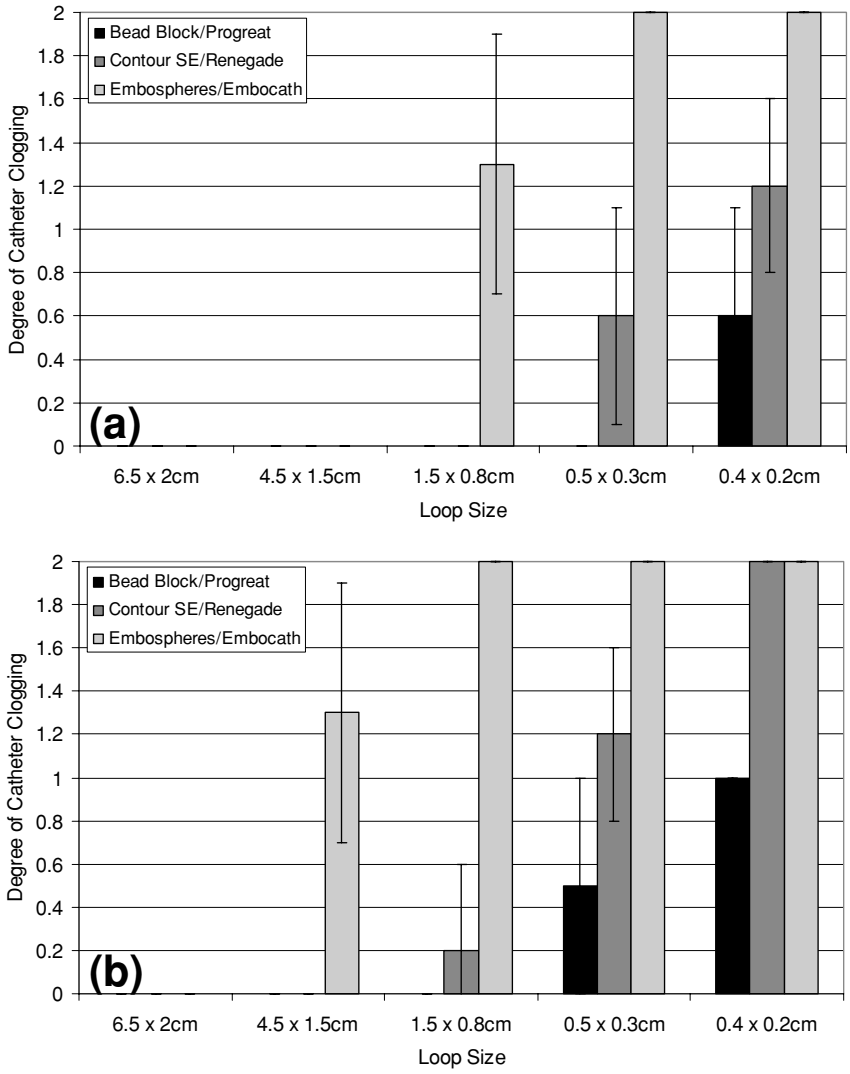

Fig. 6 Catheter deliverability: degree of clogging of embolisation agents with matched catheters (a) 500–700 μm range and (b) 700–900 μm range

3.2.2 Plasma coagulation time

Evaluation of the plasma coagulation time for each product is shown in Fig. 9. Comparison by ANOVA of the coagulation times recorded for plasma with each embolic product showed that there was a significant difference in the results. Student's t-tests confirmed that the time taken for plasma containing Bead Block to clot was significantly different from the clotting time for plasma containing Embosphere or Contour SE ($p < 0.01$), with Bead Block giving a mean clotting time of 161 seconds compared with 149 seconds for both Embosphere and Contour SE. However, the absolute difference is small. Furthermore, comparison of the samples of plasma with microspheres and without showed that none of the products tested brought about a significant change in plasma coagulation time. In each case a t-test between the microsphere-containing plasma and the control gave $p > 0.05$. This indicates that none of the products are pro-coagulatory.

4 Discussion

The distribution of microspheres within the size ranges provided was largely in line with what was quoted on the packaging for the products. The distributions obtained are mainly dictated by the manufacturing processes for the microspheres. Bead Block is made by a suspension polymerisation in which the whole size range of microspheres is made in one reaction and then the resulting products are subsequently separated through a series of sieves in order to fractionate them into the various size ranges. It is believed that the other products are sized in this way also. It is therefore anticipated that the distribution of sizes in a particular range will not necessarily fit a normal distribution. Contour SE is thought to be made by a precipitation method that produces small protrusions on the surface of the microspheres (Fig. 2(b)). Embosphere microspheres encapsulated with collagen, which occasionally results in multiple spheres entrapped within a capsule (Fig. 2(c)).

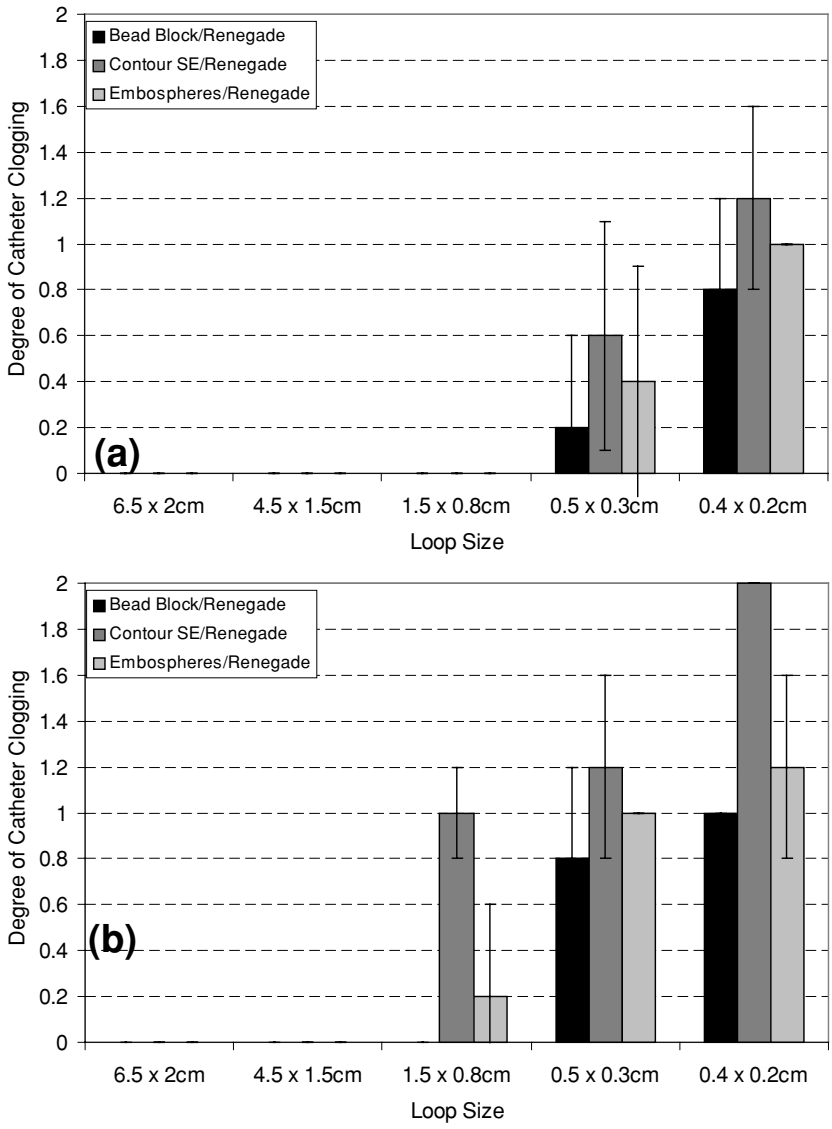

Fig. 7 Catheter deliverability: degree of clogging of embolisation agents with a fixed catheter (Renegade) (a) 500–700 μm range and (b) 700–900 μm range

In order that the microspheres can be delivered down small-bore microcatheters, they must possess some degree of compressibility. Those microspheres in the size range 900–1200 μm are not recommended for use in microcatheters by the manufacturers, although some can be delivered successfully when used with the appropriate size catheter such as 4 Fr or 5 Fr. Compressibility is particularly important for the sizes in the range 700–900 μm and 500–700 μm, as the products may need to deform in order to pass through the lumen of the catheter, especially if the catheter is contorted in any way. All of the commercial products were compressible but Contour SE in particular possesses very little resistance to compressive force. The SEM images showed that the Contour SE microspheres collapse under high vacuum and exposure of the interior structure shows that this is due to the highly macroporous nature of the microsphere. This explains why the product is not transparent to light under the microscope. The other products are hydrogel-type materials that have a high water content but do not possess a formally porous structure, and although they shrink during the preparation for SEM imaging due to loss of water, they do not collapse.

In terms of the suspension of the microspheres in contrast medium:saline mixtures, all products reach an homogeneous suspension in an acceptable time frame (between 2–4 mins), with Bead Block > Embospheres > Contour SE. More important is the time to remain in suspension as during the delivery of the product through the catheter it is desirable to inject an even suspension so as to avoid aggregation and potential blockage, and also to prevent "slugs" of embolic agent being delivered to the site of embolisation. In this case the time in suspension was in the order Bead Block $\gg$ Embosphere = Contour SE with Bead Block remaining suspended for over twice as long as the other microspheres. It should be

noted that suspension is highly dependent upon the viscosity of the solution and so varies with type of contrast agent used and the ratio of mixing with the saline. The suspension is also influenced by the size range of the microspheres selected, with larger microspheres generally sedimenting from suspension at a faster rate, (hence why the mid-range 500–700 μm microspheres were selected for study here).

When deliverability of the products was compared using the matched catheters (i.e. the catheter that would normally be made by/recommended by the supplier of the microspheres), the order of catheter clogging was seen to be Bead Block < Contour SE < Embosphere. This was seen to change to Bead Block < Embosphere < Contour SE when the Renegade catheter was selected for all product evaluations. This would suggest that the Embocath was responsible for the poorer performance of Embosphere during delivery through a tortuous catheter path, as this catheter appears to be prone to kinking when bent into too tight a loop. The high resistance to kinking of the Progreat catheter and low tendency of Bead Block to clumping made this combination the best at negotiating the tortuous path test.

Both the blood contacting SEM and the plasma coagulation time showed that none of the products were prothrombotic or pro-coagulatory. The Embosphere and Embogold products are trisacryl microspheres that are coated with collagen with a claim to aid cellular adhesion. There

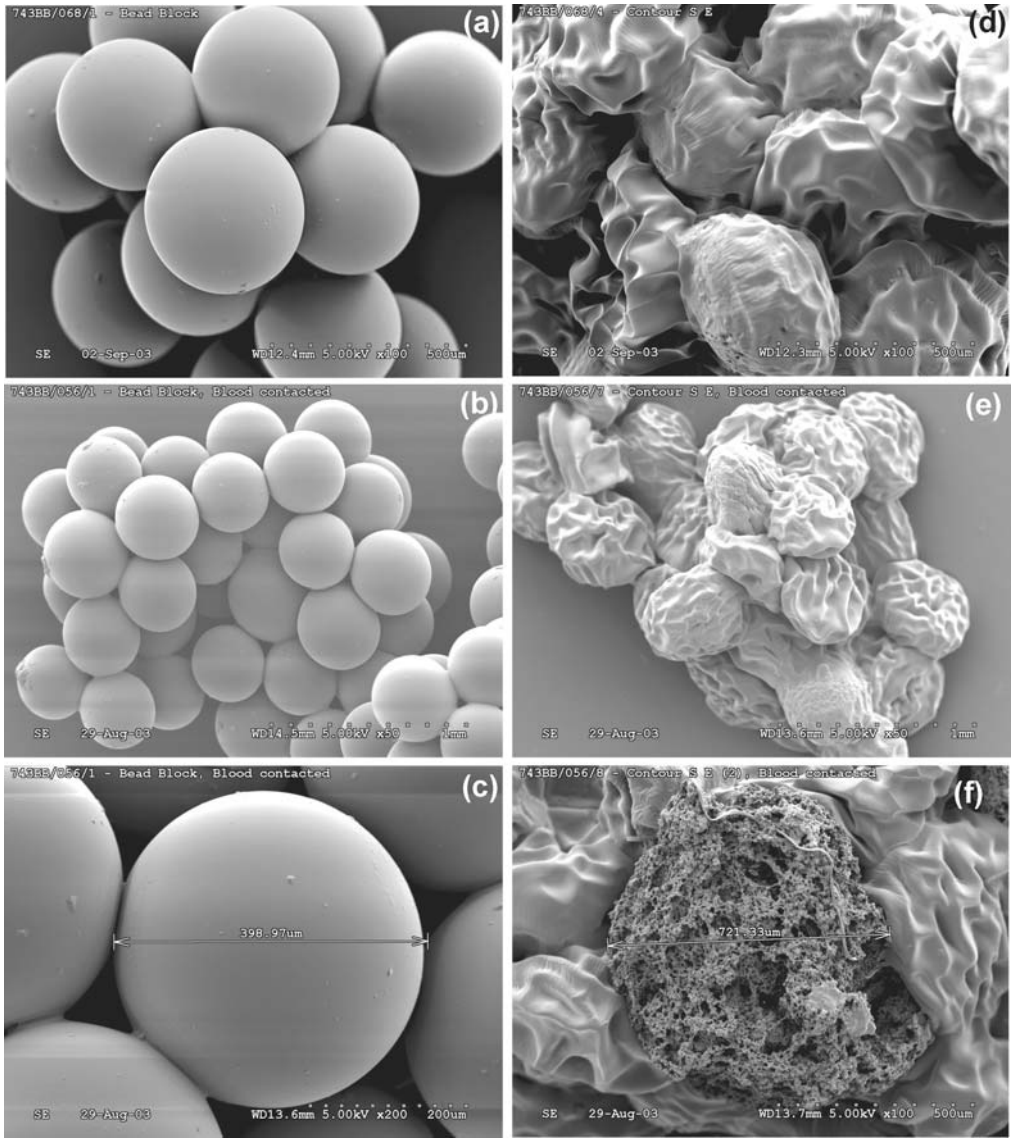

Fig. 8 Scanning electron micrographs of Bead Block (a) non blood contacted (mag × 200) (b) blood-contacted (mag × 50) and (c) blood-contacted (mag × 200); Contour SE (d) non blood contacted (mag × 200) (e) blood-contacted (mag × 50) and (f) blood-contacted (mag × 200); Embosphere Gold (g) non blood contacted (mag × 200) (h) blood-contacted (mag × 50) and (i) blood-contacted (mag × 200); Embosphere (j) non blood contacted (k) blood-contacted (mag × 50) and (l) blood-contacted (mag × 200)

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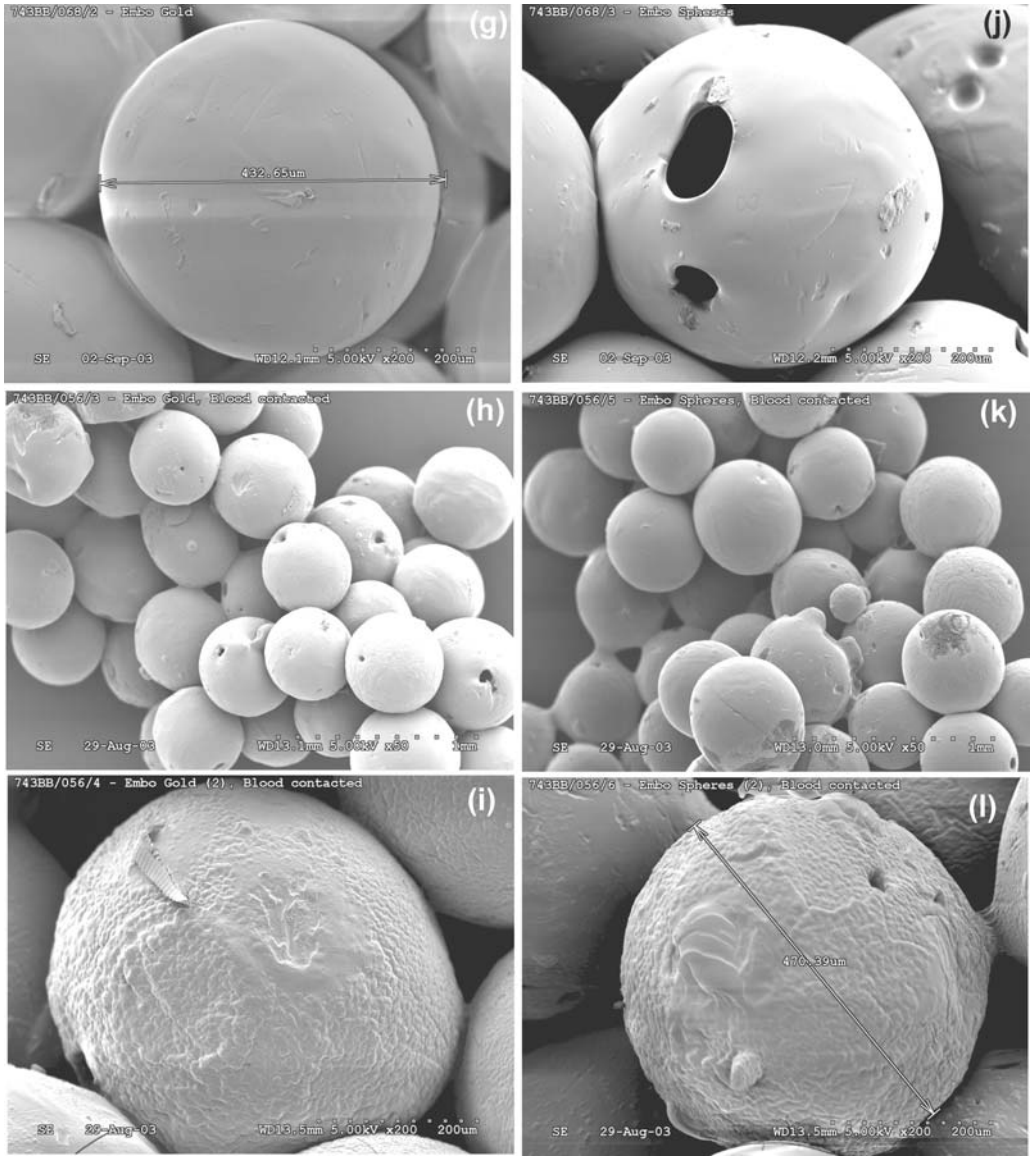

Fig. 8 (*Continued*)

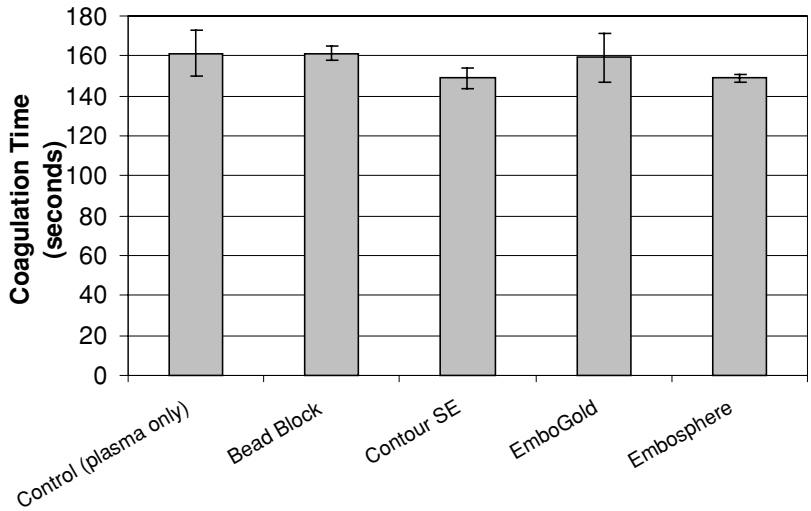

Fig. 9 Plasma coagulation times for commercial embolisation microspheres

was however, no evidence from the evaluations carried out in this study that the collagen coating conferred any additional benefit in terms of embolisation potential within the vessel.

5 Conclusions

Commercially-available microspherical embolic agents have been evaluated *in vitro* in order to compare their physical and biological characteristics. All products have been found to be largely equivalent in their overall performance in terms of calibrated size availability, suspendibility in contrast medium, ability to be delivered down microcatheters and their overall biological performance when contacted with blood. The differences observed in the product structures and hence physical properties such as compressibility will not only be important during the delivery of the product, but will also play an important part in how and where the embolic agent blocks the desired vessels. These small differences in properties will undoubtedly mean that the IR will be required to make subtle changes in the determination of a satisfactory end-point when using each of these embolic agents. Indeed, it was recommended from a recent study in a sheep kidney model that when using Contour SE it might be a consideration to use a larger size range compared to Embosphere due to differences in the level of occlusion obtained, as the Contour SE product is able to be compressed and move more distally in the vessel (deformation measured at 50.9% for Contour SE *versus* 22.4% for Embosphere ($p < 0.0001$)) [11]. Similarly, comparative *in vivo* data from liver embolisations using Embosphere and Bead Block suggest that whilst the Embosphere may clump and remain rounded in the vessel, Bead Block can deform slightly and form more of a cast within the vessel [12]. It remains to be seen whether there are advantages for one type of occlusion over another, but currently all products are being used routinely in clinical practice and perform their primary function of embolisation of target vessels.

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