LIPIODOL VISIBILITY UNDER ULTRASOUND

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BACKGROUND

Comparative studies and meta-analyses have demonstrated high concordance between HSG and HyCoSy results with respect to tubal patency, patient tolerability and adverse effects[1-4]. HyCoSy has therefore become increasingly utilised as the first-line imaging modality due to its offer of additional benefit, including the avoidance of X-ray radiation and provided simultaneous ultrasound imaging of the pelvic soft tissue.

In recent years, an asserted advantage of the use of HSG over HyCoSy in the assessment of tubal patency is the use of oil-based contrast solutions and their association with increased natural pregnancy rates post-procedure[5,6]. Systematic reviews of randomised controlled trials have indicated tubal flushing using oil-based contrast media, including procedures intended as diagnostic, was associated with increased pregnancy rates, with the greatest effect in women with unexplained sub-fertility and within six months post-procedure[7].

Oil-based agents like Lipiodol are not routinely used with ultrasound imaging and no published studies have investigated its visualisation under ultrasound. We propose that Lipiodol is not clearly visible under ultrasound in its native form, but can be visualised sonographically when agitated just prior to administration to form air microbubbles. If visibility is comparable to agitated saline, routinely utilised for HyCoSy, this provides potential for the use of Lipiodol with HyCoSy, allowing the imaging benefits associated with HyCoSy, alongside allowing the simultaneous benefit of tubal flushing with Lipiodol.

AIMS

To examine whether Lipiodol is visible sonographically, assess optimal agitated Lipiodol mix and ultrasound settings for visibility, and compare visibility to agitated saline, routinely used for HyCoSy.

MATERIALS AND METHODS

A model pelvis was constructed with a 5.3 Fr CVS catheter to represent a fallopian tube positioned 3 cm from the surface within a tofu block. The end of the catheter was accessible to introduce fluid via a three-way tap. The trans-vaginal transducer was placed on the surface of the block. Two identical GE Voluson E10 BT 18 ultrasound machines with RIC5-9D transducers were utilised, with standard GE software version EC330.

Two glass 5 mL syringes were attached via a three-way tap to the simulated fallopian tube and utilised to allow agitation of the fluid of choice, facilitating the formation of air microbubbles within the solution immediately prior to administration. One syringe was filled with 5 mL of the fluid of choice, while the other syringe was empty. Our positive control consisted of normal saline which was pumped back and forth through the two syringes five times immediately prior to administration to allow air microbubble formation, referred to as agitated saline.

Four different agitated Lipiodol mixes were tested: unmixed (Lipiodol drawn straight from the supply vial and immediately administered), mixed once (Lipiodol pumped back and forth through the two glass 5 mL syringes once prior to administering), mixed three times (Lipiodol pumped back and forth through two glass 5 mL syringes three times prior to administering) and mixed five times (Lipiodol pumped back and forth through two glass 5 mL syringes five times prior to administering). Increasing mixes allowed increasing solution agitation and consequently increasing amounts of air microbubble formation.

The test fluid was injected into each model fallopian tube by two independent doctors and two clinically experienced sonographers captured images independently, each pair utilising a separate model pelvis. Images were captured altering the dynamic range (high vs low) and harmonics (on vs off) as per the table below. Images were also captured with no fluid (negative control) and our positive control (agitated saline) using the standard ultrasound setting utilised for HyCoSy by the two sonographers (high dynamic range with harmonics on).

Each test was performed in quadruplicate and in random order. Images were read by 47 blinded reporters and visibility reported on a scale of one (not visible) to five (clearly visible).

All data were analysed using the IBM SPSS statistical package version 20 (Armonk, NY, USA) and SAS 9.4 (SAS Institute Inc., Cary, NC, USA). The scores were summarised with a mean and standard deviation. The results are presented as a risk ratio (proportion of readings >3 in each mix compared to that for saline) and a 95% confidence interval. The mean scores are compared across the mixes using a generalised linear model to account for the correlation within reporters and means were compared using a Tukey's test to keep the overall error rate at 5%.

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RESULTS

Figure 1 illustrates the proportion of visibility scores for each test. As the Lipiodol agitation increased, the greater the proportion of high visibility scores, with Lipiodol mixed five times prior to injection and image capture with ultrasound settings of 'high dynamic range and harmonics on' having the greatest proportion of reporters scoring '5 – clearly visible'. The mean visibility score for images captured where the Lipiodol sample was agitated five times prior to injection to allow the formation of air microbubbles, regardless of ultrasound setting, were higher than or not different from that for agitated saline (all $P > 0.7$ when not different, <0.001 when higher).

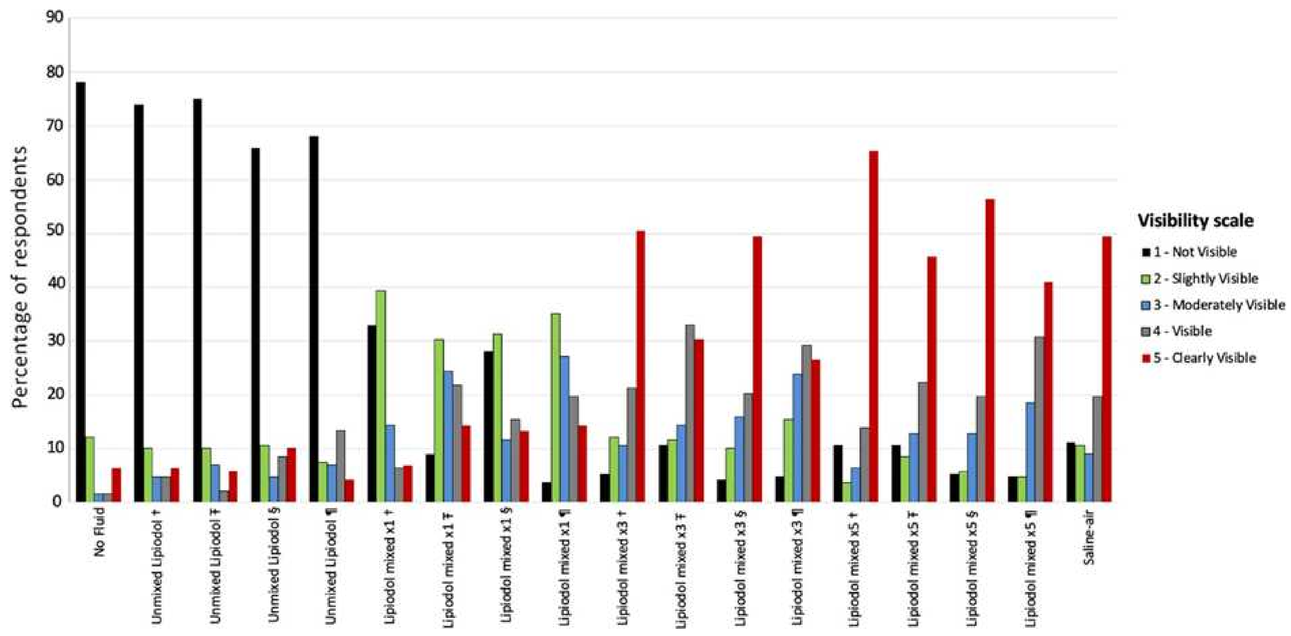
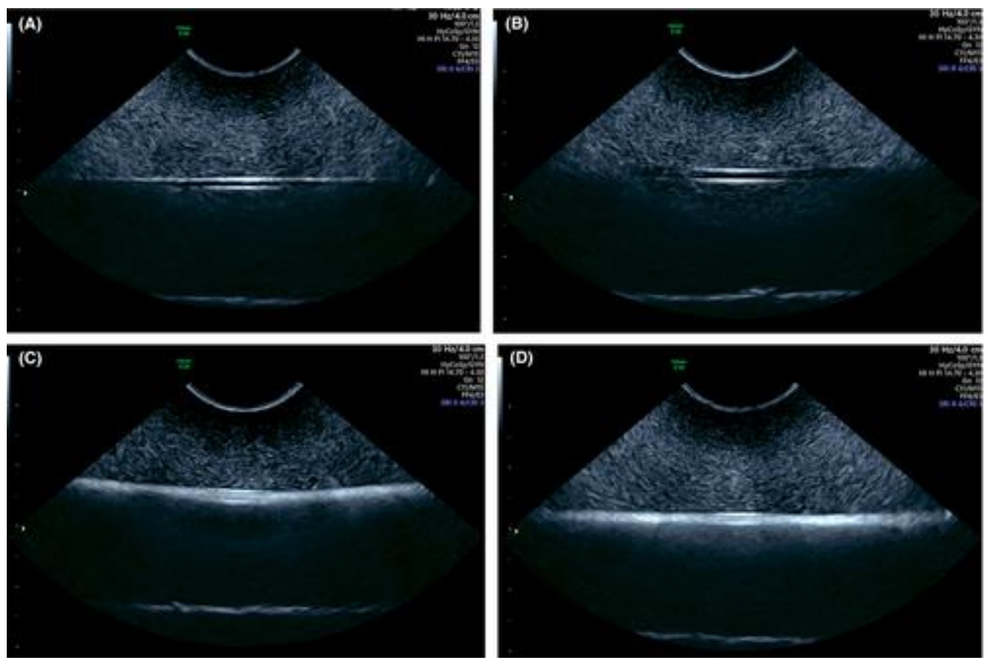


Figure 2: illustrates sample images captured with ultrasound settings 'high dynamic range and harmonics on' for (A) no fluid injected, (B) unmixed Lipiodol, (C) Lipiodol mixed five times prior to injection and (D) agitated saline.



CONCLUSION

We have provided the first published evidence that agitated Lipiodol is visible under ultrasound imaging, and that visibility is similar or better than agitated saline, ubiquitously used for HyCoSy. We have also demonstrated that these results were reproducible regardless of sonographer or reporter.

The benefit of the ability to perform HyCoSy with Lipiodol is the circumvention of radiation exposure that occurs with HSG, in addition to allowing simultaneous ultrasound imaging of pelvic pathology. Important in infertility evaluation, trans-vaginal sonography provides the ability to comprehensively evaluate the soft tissue within the pelvis including assessment of the myometrium, endometrial lining and ovarian architecture. This allows visualisation of soft-tissue abnormalities within the uterus and pelvis, such as fibroids, adenomyosis and adnexal pathology, in addition to intrauterine pathology.

Lipiodol may therefore present a possibility for use with HyCoSy, with the added benefit of oil-based tubal flushing, avoiding the radiation exposure of HSG and concurrently providing pelvic soft-tissue evaluation.

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