A prospective study of multiple needle biopsies versus a single open biopsy for testicular sperm extraction in men with non-obstructive azoospermia*

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Little is known about the efficacy and the factors affecting the outcome of fine needle aspiration biopsy of the testis for sperm retrieval in azoospermic men with defective spermatogenesis. A prospective study was designed to compare the efficacy of needle and open (window) testicular biopsies for testicular epididymal sperm extraction (TESE) in 35 consecutive men with azoospermia due to defective spermatogenesis undergoing testicular biopsy for intracytoplasmic injection of oocytes. Each of the consecutive 35 patients underwent TESE using a 19 gauge butterfly needle followed by a window (1–1.5 cm-sized incision) testicular biopsy in the same procedure. The extraction of spermatozoa into culture medium was compared with the assessment of testicular biopsies by histology, the mode of biopsy (needle or open biopsy) and the amount of tissue retrieved by either method. Testicular spermatozoa were retrieved in 22 (63%) who had an open testicular biopsy compared with five (14%) patients who had multiple needle biopsies, respectively; the difference was statistically significant. Open testicular biopsy retrieves more testicular tissue than needle biopsy. Needle testicular biopsy retrieved testicular spermatozoa in 50% of those with hypospermatogenesis, 10% with focal spermatogenesis and in no patients with maturation arrest or Sertoli cell-only pattern. In contrast, sperm retrieval was successful in 100%, 90% and 66% of those with respective histologies using open testicular biopsy. Other than bruising, for which they required no analgesia, none of the patients suffered any obvious complications associated with traditional testicular biopsy. We conclude that open testicular biopsy is more effective than needle biopsy for the retrieval of testicular spermatozoa in azoospermic men with defective spermatogenesis. The difference observed may be related to the amount of testicular tissue retrieved and to the influence of testicular histology.

Key words: needle biopsy/non-obstructive azoospermia/TESE

Introduction

The technique of intracytoplasmic sperm injection (ICSI) has made possible the treatment of men with azoospermia due to defective spermatogenesis. These patients may have cryptozoospermia and so some spermatozoa may be found on the day of ovum retrieval from a careful search in their ejaculate without resorting to testicular sperm extraction (TESE). Nagy et al. (1995) reported an ongoing pregnancy rate of 24.5% per cycle in 57 cycles in the wives of men with cryptozoospermia which is similar to what is reported for ICSI with testicular and epididymal spermatozoa or ejaculated spermatozoa from men with normozoospermia (ESHRE, 1997). However, cryptozoospermia occurs in only 9.8% of patients with azoospermia (Lindsay et al., 1995). Moreover, cryptozoospermia may be intermittent with the result that ejaculated spermatozoa may not be found on the day of egg retrieval. Although normal births have been achieved with ejaculated spermatids, many problems mitigate against the success rates and the wider application of spermadit microinjection (Sousa et al., 1998). Testicular spermatozoa are therefore the main germ cell used for ICSI in men with azoospermia due to defective spermatogenesis. However, access to testicular spermatozoa requires a testicular biopsy, which may be associated with significant potential complications (Beierdorffer and Schirren, 1979; Schlegel and Su, 1997). Although reducing the size of the testicular incision may minimize these complications, needle biopsy is a quicker, simpler and less invasive procedure compared to an open testicular biopsy (Mallidis and Baker, 1994; Gottschalk-Sabag, et al., 1995; Harrington et al., 1996). These enormous advantages gave needle biopsy considerable popularity as a means of assessing the status of spermatogenesis in the testis in an outpatient setting (Mallidis and Baker, 1994; Craft et al., 1997) and made percutaneous epididymal sperm aspiration (PESA) a viable alternative to microsurgical epididymal sperm aspiration (MESA) for gamete retrieval in men with obstructive azoospermia (Craft and Tsirigotis, 1995; Collins et al., 1996). Nevertheless, little is known about the effectiveness of a needle biopsy in recovering testicular spermatozoa in azoospermic men with defective spermatogenesis. The focal nature of spermatogenesis in men with azoospermia due to defective spermatogenesis (Tournaye et al., 1996) has led to the speculation that multiple needle biopsies could retrieve more spermatozoa than a single open

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testicular biopsy (Craft and Tsirigotis, 1995), but only a few studies have investigated this claim under controlled circumstances (Friedler et al., 1997; Turek et al., 1997). In addition, the factors affecting the outcome of fine needle aspiration biopsy of the testis for sperm retrieval in azoospermic men with defects in spermatogenesis is unknown. We have looked for evidence in support of this hypothesis by comparing multiple fine needle biopsies with an open biopsy for TESE in men with azoospermia due to defective spermatogenesis.

Materials and methods

Patient selection
Thirty-five consecutive patients with azoospermia due to defective spermatogenesis scheduled for testicular biopsy for genetic studies and later for intracytoplasmic injection of the oocyte were studied. Testicular biopsies and sperm extraction were not synchronized with oocyte retrieval and ICSI cycles which were performed 3–6 months later. Testicular spermatozoa obtained were cryopreserved. The study was approved by the South Sheffield Hospital Ethics Committee. Semen samples were collected and analysed according to the World Health Organization (1992) criteria. The diagnosis of azoospermia was made after no spermatozoa were found in the pellet obtained from semen centrifuged at 1500 g for 10 min. The developmental, social, medical and reproductive histories as well as history of urological operations and exposure to gonadotoxins were documented. Each patient underwent general, systemic and genital examinations. Testicular volume was estimated with a Prader orchidometer. The plasma concentrations of follicle stimulating hormone (FSH) (normal value: 1–2 IU/l) and luteinizing hormone (LH) (normal value: 2–11 IU/l) were determined by enzyme linked immunooassay. Plasma testosterone (normal value: 9.4–37.0 nmol/l) was analysed by radio-immunoassay (Diagnostic Products Ltd, Cardiff, Wales, UK). The intra- and interassay coefficients of variation did not exceed 6.5%. A chromosomal analysis of a venous blood sample was also carried out for each patient using standard techniques prior to testicular biopsy. The Y-chromosome microdeletion assay was not performed on any of the patients. Where genital cystic fibrosis (CF) was suspected because of low sperm volume, acidic pH or absence of vasa deferentia, a cascade screening of common CF gene mutations was undertaken to help in the exclusion of those with obstructive azoospermia. Azoospermic patients suspected clinically to have retrograde ejaculation, obstruction of the genital tract and endocrine disorders were excluded from the study. Only patients judged clinically to have azoospermia due to defective spermatogenesis (testicular atrophy, raised plasma FSH, exposure to gonadotoxins such as radiotherapy and chemotherapy, chromosomal abnormality, mumps orchitis, testicular torsion) were studied.

Study design
The study was designed in such a way that each patient could act as his own control. To achieve this objective each of the patients had multiple needle testicular biopsies followed by an open biopsy in the same procedure from the site of the needle biopsy. All the testicular biopsies were performed by the same surgeon. Unilateral open testicular biopsy was taken from the larger of the two testes.

Testicular biopsy

Anaesthesia
The first 19 patients had general anaesthesia and subsequent patients outpatient analgesia. Outpatient analgesia comprised sedation with i.v. midazolam, spermatic cord block with 0.5% bupivacaine solution and local infiltration of the scrotum with 2% lignocaine in a 1:200 000 adrenaline solution.

Multiple needle testicular biopsies
The scrotal region was shaved before surgery, and the skin of the groin was cleaned with an aqueous solution of 0.1% chlorhexidine and draped in such a way as to expose only the testicles. Genital examination was performed to confirm the findings at the clinic. The anterior scrotal skin was stretched and the testicle held with the left hand in such a manner as to maintain the epididymis in the posterior position. Using the right hand, the larger of the two testes was punctured with a 19-gauge butterfly needle attached to a 20 ml syringe whose plunger was drawn to a 15 ml mark in order to create a strong negative pressure. The needle was pushed in five different directions (anteriorly, posteriorly, forwards and backwards and inferiorly) while maintaining suction. A pair of artery forceps was secured across the attached microtubbing prior to withdrawing the butterfly needle from the testis and scrotal skin. Any tissue left on the skin in the needle tract was recovered with a pair of forceps. The artery forceps were removed and the plunger released to discharge any tissue from the butterfly needle into a Petri dish. The contents of the syringe and needle were washed out with Earle’s balanced salt solution (EBSS) to remove any tissue or spermatozoa in the syringe.

Open window (simple) testicular biopsy
With the right hand, a 1–1.5 cm incision was made on the convexity of the centre of the anterior portion of the larger testis, through the point of entry of the needle, and through the skin, tunica vaginalis and tunica albuginea, with a size 11 scalpel blade. Gentle pressure on the testis extruded a small amount of testicular parenchyma from the incision. A piece of testicular tissue, measuring between 0.5×1.0×0.5 cm and 1.0×1.5×1.5 cm, was excised with a wet, sharp pair of curved iris scissors, for histopathological analysis. A similar amount of tissue was removed for sperm extraction. Haemostasis was secured with electrocautery. The tunica albuginea and tunica vaginalis were closed in layers with a continuous 3/0 vicryl suture. The skin was closed with a subcuticular 3/0 vicryl stitch. A Pethadine wound spray, and a dry scrotal dressing were then applied. Tissues for histology were placed in a pot containing Bouin’s solution and those for TESE in a Petri dish containing phosphate-buffered saline (PBS) and immediately transported to the laboratory.

Discharge and follow-up
The patients stayed in the recovery room for 30–90 min and went home on recovery from anaesthesia. No antibiotics or pressure scrotal dressings were applied. Patients were advised to keep the area dry and to report any bleeding, discharge or swelling. They were seen 2 weeks after the procedure, and enquiries were made about pain, swelling, infection and intercourse. Testicular volume was estimated with a Prader orchidometer and the biopsy sites were examined.

Testicular sperm extraction
The TESE procedure was the same process for both the percutaneous pieces and the open pieces. A piece of biopsy tissue was minced into fine pieces with two sterile microscopic glass slides and transferred in PBS to a conical centrifuge tube (Falcon type, 100 mm; Fahrenheit Laboratory Supplies, Rotherham, UK), vortexed for 5 min, and centrifuged for 5 min at 500 g. The pellet was resuspended for 5 min in 2 ml of erythrocyte-lysing buffer and allowed to stand for 5 min. After centrifugation at 500 g for 5 min, the pellet was resuspended in EBSS medium and transferred to a Petri dish containing 3 ml of EBSS. The medium was overlaid with 1 ml paraffin oil. The preparation was examined for the presence of testicular spermatozoa immediately and then incubated at 37°C in an atmosphere of 5%
CO₂, in air for up to 72 h. This testicular culture was examined each day for the presence of testicular spermatozoa.

**Testicular sperm cryopreservation**

Purified spermatozoa were diluted dropwise 1:3 (e.g., 1 ml cryoprotectant medium:3 ml spermatozoa = 0.33 ml cryoprotectant medium:1 ml spermatozoa) with the freezing medium (Irvine Scientific, California USA). Spermatozoa were loaded in the plastic straws (0.5 ml; Rocket, London, UK), which were sealed by dipping the ends of the straws into some Scant powder (Rocket) in a test tube and subsequently into ultra high purity water after wiping off excess powder with a tissue. The straws were cooled and stored as described by Verheyen et al. (1997). The testicular tissues containing spermatozoa were cryopreserved in cryovials. The outcome of cryopreservation of testicular tissues and purified spermatozoa is not reported in this paper.

**Histopathology**

Pieces of testicular biopsy were fixed immediately in Bouin’s solution. Semi-thin paraffin wax sections (4 μm) were stained and examined by light microscopy at ×400 magnification using standard techniques. The slides were read by three different assessors unaware of the results of the TESE or identification of round spermatids. Testicular histology was classified into hypospermatogenesis (reduction in the degree of normal spermatogenic cells), maturation arrest (an absence of the later stages of spermatogenesis), Sertoli cell-only (the absence of germ cells in the seminiferous tubules) and focal spermatogenesis (small areas of apparently normal spermatogenesis). Testicular histology was scored on a scale of 1–10 according to the method of Johnsen (1970). The histology was performed only on open biopsy samples to maximize the use of needle biopsy samples for TESE.

**Main outcome measures**

The type of biopsy (needle or open) was used as predictor of testicular histological patterns and of retrieval of at least one testicular spermatozoon.

**Statistical analysis**

Paired categorical variables were compared with McNemar’s test. Differences between median values were tested using the Mann–Whitney U-test. Values are presented as two sided P-values with 95% confidence intervals. P < 0.05 was judged as statistically significant. It was estimated that 32 patients would be adequate for the study with the power set at 80%, α at 0.05 and the difference in efficacy between needle and open biopsy set at 40%.

**Results**

All the 35 patients underwent TESE. Patients with primary gonadal failure were selected on clinical criteria and testicular histology confirmed this diagnosis in all the patients. The mean plasma FSH concentration was 18.5 IU/l (SD: 12.5) and testicular volume 30.4 ml (SD: 12.4). Tissues retrieved with open biopsy measured 0.5×1.0×0.5 cm to 1.0×1.5×1.5 cm compared to tiny, thread-like tissue and fluid obtained with needle biopsy. Testicular spermatozoa were recovered in 22 of 35 patients, giving a sperm retrieval rate of 63%.

Table I compares the efficacy of needle with open testicular biopsy. Both needle and open testicular biopsies retrieved testicular spermatozoa in five (14%) patients but failed to do so in 13 patients. There was no case where needle biopsy retrieved testicular spermatozoa without open testicular biopsy doing so. In contrast, open testicular biopsy retrieved testicular spermatozoa in 17 patients where needle biopsy failed. There was a statistically significant difference in sperm retrieval rate between multiple testicular biopsies and an open testicular biopsy. (McNemar’s χ² = 16.056, df = 1; P < 0.0001).

Hypospermatogenesis was reported in eight patients, focal spermatogenesis in nine, maturation arrest in seven and Sertoli cell-only in 11. Sperm retrieval was higher in patients with hypospermatogenesis and focal spermatogenesis compared with the groups with maturation arrest or Sertoli cell-only pattern (Table II). Needle biopsy succeeded in retrieving testicular tissue spermatozoa only in 50% of patients with hypospermatogenesis and 10% with focal spermatogenesis (Table II). Those with successful sperm extraction using both needle and open testicular biopsy had Johnsen’s scores of 9.0, 9.1, 8.3, 8.2 and 5.8 but sperm extraction failed using needle biopsy in four patients with hypospermatogenesis and Johnsen scores of 7.8, 8.8, 7.5 and 7.9.

Testicular spermatozoa were not retrieved from the two patients who had Klinefelter’s syndrome. Spermatozoa were retrieved from two patients with Y-chromosome deletion and another two with chromosome translocation. Others had a normal karyotype. Testicular volume and plasma FSH, LH and testosterone concentrations did not predict testicular sperm retrieval (P > 0.05).

One patient with testicular atrophy bled more than usual, and bleeding was controlled with diathermy. In another patient with testicular atrophy the testis slipped out of the operating field, and was brought into view with some difficulty. The use of a stay suture on the tunica albuginea prevented the recurrence of this problem. All the patients felt bruised at the site of the biopsy but this symptom diminished remarkably after 3 days, and none of the patients required analgesia. None of the patients suffered scrotal wound infection or haematoma. In all cases the wound was well healed by the 10 days when they were reviewed. Coitus was resumed within 1 week of the operation in all patients. There was no change in testicular size, as measured with an orchidometer, both before and after the operation.

**Discussion**

We found that a simple open testicular biopsy is more effective than multiple fine needle aspiration biopsies in retrieving spermatozoa from the testes of men with azoospermia due to defective spermatogenesis (non-obstructive azoospermia). The

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<th>Needle biopsy for TESE in azoospermia</th>
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<td><strong>Table I. Testicular sperm extraction according to the type of biopsy</strong></td>
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<td><strong>Needle biopsy</strong></td>
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<tr>
<td>Success</td>
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<tr>
<td>Open biopsy</td>
</tr>
<tr>
<td>Failure</td>
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<td>Total</td>
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Values are number of patients with successful or failed testicular sperm extraction.

* versus †: P < 0.0001 (McNemar’s test).
diagnosis of non-obstructive azoospermia was made clinically and subsequent histological examination confirmed this diagnosis in all the patients.

Previous studies evaluating the use of needle testicular biopsy were mainly for the assessment of spermatogenesis in the testis. Biopsy samples obtained with fine needle aspiration biopsy have been found to show a good correlation with conventional histology obtained by open biopsy (Mallidis and Baker, 1994; Craft et al., 1997). However, the efficacy of fine needle aspiration biopsy in retrieving testicular tissue adequate for histological analysis may depend on the pathology of the testis. Mallidis and Baker (1994), having a higher proportion of patients with non-obstructive azoospermia, reported a high incidence of histological artefacts in 45% of cases with fine needle aspiration biopsy. On the other hand, Craft et al. (1997), who did not have patients with maturation arrest in his series, reported a 100% correlation between fine needle aspiration and open testicular biopsies. Fine needle aspiration biopsy is increasingly being used for TESE in patients with azoospermia (Bourne et al., 1995, Craft and Tsirigotis, 1995). In 7% of patients with obstructive azoospermia, TESE is required because epididymal sperm retrieval has failed due to epididymal scarring or retrieval of dead epididymal spermatozoa (Schosyman et al., 1993). A retrospective study comparing the mode of testicular recovery with the outcome of ICSI in patients with obstructive azoospermia with normal spermatogenesis showed that both open and fine needle aspiration biopsies give similar results in terms of the number of samples per puncture and spermatozoa retrieved as well as fertilization, cleavage, pregnancy and implantation rates (Tournaye, 1998).

We have previously reported the outcome of TESE in 19 patients with non-obstructive azoospermia; spermatozoa were retrieved with needle biopsy from only one (5%) patient and with open biopsy in 11 (58%) patients (Ezeh et al., 1996). Our present study, involving more patients and relating the testicular pathology to the type of testicular biopsy, confirms our earlier findings. The findings of our study are similar to those of a recent study by Friedler et al. (1997) comparing multiple needle and multiple open testicular biopsies in 37 patients, in which testicular spermatozoa were retrieved with needle biopsy in four (11%) patients and open biopsy in 16 (43%). There are a number of differences between their study and this study. First, our study compared multiple needle biopsies and a single testicular biopsy. In spite of this, our sperm retrieval rate of 63% is higher than 43% reported by these authors. A difference in the method of sperm extraction may account for this disparity. Whereas fine mincing of testicular tissues and immediate examination of testicular tissues for spermatozoa were used in their study, we combined this procedure with the use of erythrocyte-lysing buffer and in-vitro culture of testicular tissues. Second, the effect of the type of testicular histological patterns and values of Johnsen score on the mode of testicular biopsy were explored in our study. Third, we used a 19-gauge needle which is bigger than the 21-gauge needle used in that study. However, the findings of our study contrast with those of Turek et al. (1997) who compared 34 paired matched sites (open versus fine needle aspiration) in 12 patients with non-obstructive azoospermia. Multiple fine needle aspiration biopsies were found to be as effective as multiple open biopsies in retrieving mature testicular spermatozoa (McNemar’s test: P = 0.25) and in four out of 12 (33%) patients multiple fine needle aspiration biopsies detected spermatozoa in areas distant from sperm-negative biopsy sites, supporting the hypothesis that spermatogenesis in men with non-obstructive azoospermia is focal (Turek et al., 1997). Whereas it is well established that sperm production is deficient in patients with non-obstructive azoospermia, how spermatogenesis is distributed in their testes is debatable. Silber et al. (1997) recently proposed a homogeneous and multifocal rather than a patchy distribution of spermatogenesis proposed by Tournaye et al. (1996). A major criticism of the proposed testis mapping procedure is the potential for injuries from numerous blind needle passes required to map the testis (Obl, 1997). Schlegel and Sul (1997) have drawn attention to the injuries that can be inflicted on the testis due to devascularization and inflammatory changes following testicular biopsy, even when the testis looks clinically normal post-operatively. Harrington et al. (1996) have shown that such injuries could occur in 7% of patients undergoing a single needle biopsy. It is therefore conceivable that greater injuries may occur following multiple blind needle passes to map the testes. The reason why the results of Turek et al. (1997) are different from the findings of others (Friedler et al., 1997) and of this study is not known. It is possible that the difference in the study population size and the fact that multiple open and fine needle aspiration biopsies were performed at different times in some patients during the testicular mapping technique may be responsible. Turek et al. (1997) specified neither the amount of testicular tissue obtained with open and fine needle aspiration biopsies nor the size of incision made on the testis. The amount of testicular tissue retrieved affects the testicular sperm retrieval rate (Schlegel et al., 1997). We doubt that the difference between the outcome of the two studies could be attributed to the difference in needle size since the 19-gauge needles used in this study are bigger than the 21-gauge needles used by Turek et al. (1997). This is because the larger the

<table>
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<th>Histological diagnosis</th>
<th>Johnsen score Median (range)</th>
<th>Needle biopsy No. (%)</th>
<th>Open biopsy No. (%)</th>
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<tr>
<td>Hypospermato genesis</td>
<td>8.6 (7–9)</td>
<td>4 (50)</td>
<td>8 (100)</td>
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<tr>
<td>Focal spermatogenesis</td>
<td>6.1 (4.8–7.7)</td>
<td>1 (10)</td>
<td>9 (90)</td>
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<tr>
<td>Maturation arrest</td>
<td>3.1 (2.4–5)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sertoli cell-only</td>
<td>2</td>
<td>0 (0)</td>
<td>6 (55)</td>
</tr>
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gauge of the needle the more the testicular spermatozoa are retrieved (Bruning et al., 1995).

Our sperm retrieval rate is similar to the 62% rate reported by Schlegel et al. (1997), who used almost exclusively a single large biopsy, but higher than the 50% rate reported by Tournaye et al. (1996) who used small multiple biopsies, despite the fact the both groups used a similar method of TESE. This suggests that the aggregate size of tissue retrieved may be as important for sperm retrieval as the site of biopsy. Fine needle aspiration biopsy is inferior to an open biopsy in the evaluation of seminiferous tubule and interstitial tissue architecture, the number of seminiferous tubules retrieved, Johnsen score or the number of spermatids per tubule (Gottschalk-Sabag et al., 1995; Harrington et al., 1996). The amount of tissue obtained during an open biopsy in our study was far greater than that retrieved with multiple fine needle aspiration biopsies when mostly fluid was obtained. Perhaps the larger the tissue obtained at biopsy the more likely that seminiferous tubules with normal spermatogenesis are included in the biopsy sample for sperm retrieval. We therefore believe that the amount of testicular tissue obtained, and the fact that needle biopsy is a less efficient technique than an open testicular biopsy, could explain why multiple testicular needle biopsy which would appear to reach a wider area of the testis, failed to retrieve spermatozoa in 17 (49%) cases where an open testicular biopsy was successful. The difference in the outcome of sperm retrieval with fine needle aspiration biopsy in men with obstructive azoospermia with normal spermatogenesis and azoospermic men with deficient spermatogenesis suggests that testicular pathology also affects the efficacy of fine needle aspiration biopsy in retrieving testicular spermatozoa.

Our study shows that sperm retrieval rate is higher in patients with hypospermatogenesis compared to those with Sertoli cell-only. This confirms the findings of Jow et al. (1993), which showed sperm retrieval rates of 64% for hypospermatogenesis, 23% for maturation arrest and 0% for Sertoli cell-only, and Friedler et al. (1997) who found rates of 50%, 25% and 45% for the respective histologies. It is also in agreement with the findings of Tournaye et al. (1996) that patients with hypospermatogenesis and focal spermatogenesis needed fewer testicular biopsies and yielded more spermatozoa than those with maturation arrest or Sertoli cell-only patterns. Patients with hypospermatogenesis having relatively many areas of normal spermatogenesis yielded spermatozoa with either of the techniques, unlike those with more severe impairment of spermatogenesis. The fact that sperm retrieval was possible in only 50% of patients with hypospermatogenesis using needle testicular biopsy suggests that the probability of sperm retrieval with needle biopsy may depend on the severity of hypospermatogenesis. But the poor correlation observed between the Johnsen score and the outcome of needle biopsy in those with hypospermatogenesis and focal spermatogenesis suggests that the status of the seminiferous tubule retrieved rather than the type of histology per se may be critical to successful sperm extraction with needle biopsy.

None of our patients needed prophylactic antibiotics or scrotal support. Potential side-effects of the traditional open biopsy required for testicular exploration include primary and reactionary haemorrhage, post-operative pain, haematoma formation and infection which have been reported to be associated with testicular biopsy (Beierdorffer and Schirren, 1979). Although some of our patients suffered only bruising and minor discomfort similar to those which were reported for needle biopsy (Malidis and Baker, 1994), none developed any of these major complications probably because of the small skin incision (1–1.5 cm) needed to extract testicular tissue. However, the potential for subclinical vascular injuries to the testis remains (Schlegel and Su, 1997). We chose a single portal of entry to the testis with the needle because we felt that this would cause less post-operative pain than multiple entry sites and would minimize damage to subcapsular end arteries that perforate the tunica albuginea which supplies the testicular parenchyma (Schlegel and Su, 1997). Taking the needle biopsy from the same site as the open biopsy minimizes the chances of bias in this study.

In conclusion, open tissue extraction in patients with azoospermia due to defective spermatogenesis is safe and is superior to multiple fine needle extraction in terms of testicular sperm recovery. The observed difference in outcome between the two techniques may be attributed to the difference in the amount of testicular tissue obtained and the influence of testicular pathology. Open testicular biopsy should become the method of choice for sperm retrieval in patients with azoospermia due to defective spermatogenesis. Further studies are needed to relate the viability of testicular spermatozoa and the outcome of ICSI with the mode of testicular sperm retrieval.

Conflicts of interest
The authors wish to declare that there was no vested interest of a commercial nature such as directorships, large-scale shareholdings, substantial fees received from a commercial or other company, and large gifts or perks such as travel or holidays, involved with undertaking this research.

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