# Technetium-99m-DMSA Renal Cortical Scintigraphy to Detect Experimental Acute Pyelonephritis in Piglets: Comparison of Planar (Pinhole) and SPECT Imaging

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The purpose of this study was to directly compare the sensitivity and specificity of SPECT and pinhole imaging for the detection of acute pyelonephritis using histology as the standard of reference. **Methods:** Bilateral vesicoureteral reflux of infected urine was induced in 16 piglets (32 kidneys) by unroofing the intravesical ureter and subsequently instilling a broth culture of *E. coli* into the bladder. DMSA scans were obtained by both pinhole and SPECT techniques at 24 hr (4 piglets), 48 hr (5 piglets), 72 hr (4 piglets) and 10 days (3 piglets) after instillation of bacteria into the bladder. Kidneys were harvested immediately after scintigraphy for histopathologic examination. Results of the SPECT images, pinhole images and histologic findings were interpreted independently in a blinded fashion. The images of each kidney were classified as positive or negative for pyelonephritis regardless of the severity and number of lesions. To evaluate accuracy of SPECT and pinhole imaging for the detection of individual lesions, each kidney was arbitrarily divided into three zones (upper, middle and lower). Image findings were then compared with the pathology results for the presence or absence of pyelonephritis in each zone. **Results:** Histopathology revealed pyelonephritis in 24 of 32 kidneys (58 of 96 zones). The sensitivity of the DMSA scan for detection of affected kidneys was 92% for SPECT and 83% for pinhole; overall accuracy was 88% for both. The sensitivity of SPECT for the detection of affected renal zones was slightly better than pinhole imaging (91% compared with 86%), but its specificity was lower (82% compared with 95%) resulting in a similar accuracy. Excluding four piglets where scans were obtained within 24 hr after instillation of bacteria into the bladder, the sensitivity of SPECT and pinhole for the detection of affected kidneys were 95% and 90%, respectively. Their overall accuracy were 96% and 92%. In this subgroup, the sensitivity, specificity and accuracy of SPECT for the detection of involved zones were 96%, 95% and 96%, respectively. The corresponding values for pinhole imaging were 90%, 95% and 92%, respectively. **Conclusion:** Although the sensitivity of SPECT for the detection of acute pyelonephritis is slightly better than pinhole DMSA scan, the overall accuracy of these two imaging techniques is essentially the same.

**Key Words:** pyelonephritis; technetium-99m-DMSA; SPECT; pinhole magnification

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Technetium-99m-DMSA renal cortical scintigraphy using planar imaging has been shown to be a sensitive and reliable technique in the detection and localization of experimental acute pyelonephritis in piglets (*1,2*). With the introduction of multidetector gamma cameras and the refinement in SPECT technology, SPECT of DMSA renal cortical scintigraphy became available as an appealing clinical tool for the detection of acute pyelonephritis. Comparative studies of SPECT and planar (pinhole) techniques in children have been reported to show SPECT to be significantly more sensitive than pinhole imaging in the detection of cortical "defects" (*3,4*). In these clinical studies, however, there is no confirmation of the nature of the cortical defects which were seen on the SPECT image and not seen on the pinhole images, raising the possibility that some of these defects might be artifacts or normal variants. The purpose of this study was to compare the sensitivity and specificity of SPECT and pinhole DMSA scans for the detection of acute pyelonephritis.

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## MATERIALS AND METHODS

### Experimental Model

Bilateral vesicoureteral reflux was surgically produced in 18 Yorkshire male piglets (2–4 wk of age) by incising the roof of the intramural ureter back to the ureterovesical junction. Postoperatively the piglets were kept on antibiotic prophylaxis for five days using trimethoprin-sulfamethoxazole (Bactrim) to keep the urine sterile during the healing period. Antibiotics were then discontinued, and 2–5 days later a urine sample was obtained for culture by suprapubic aspiration. Urinary infection was then induced by the percutaneous introduction into the bladder of approximately 10 cc of a broth culture of *E. coli* as well as 1–2 cc of molten paraffin wax to function as a foreign body, a condition necessary to maintain infection. Two piglets died before imaging. The remaining 16 piglets (32 kidneys) were divided into four groups and imaged at 1, 2, 3 or 10 days after the introduction of the bacteria into the bladder (Table 1).

### DMSA Scintigraphy

SPECT and planar images of the kidneys were obtained 2–3 hr after intravenous injection of 1 mCi (approximately 100 $\mu$Ci/kg) $^{99m}$Tc-DMSA. A small field of view gamma camera was used for planar imaging. A posterior image encompassing both kidneys was obtained using an ultrahigh resolution parallel-hole collimator. Magnified images of each kidney were then obtained in posterior and posterior-oblique projections using a pinhole collimator with a 3-mm aperture.

SPECT images were obtained using a dual-head detector gamma camera equipped with ultrahigh resolution collimators. The images were acquired on 128 × 128 matrix, using a noncircular motion at 3° increments and 30 sec of scanning time per stop. A total of 120 projectional images (60 images per detector) were obtained. SPECT images were stored under code names. Immediately after completion of DMSA scintigraphy, the piglets were killed and their kidneys were removed for histopathologic examination.

**TABLE 1**
Histologic Evidence of Pyelonephritis in 24 of 32 Kidneys (58 of 96 renal zones) Exposed to Reflux of Infected Urine

| Exposure (days) | No. of kidneys | Pyelonephritis | |
|---|---|---|---|
| | | Kidneys | Zones |
| 10 | 6 | 6/6 | 18/18 |
| 3 | 8 | 5/8 | 13/24 |
| 2 | 10 | 9/10 | 20/30 |
| 1 | 8 | 4/8 | 7/24 |

### Histopathologic Evaluation

Formalin was introduced into the renal pelvis through the ureter before immersion in the fixative. The kidney was bivalved along its longitudinal axis and sections were obtained at 1- to 2-cm intervals from the upper, middle and lower segments of each half of the kidney for a total of 12 sections from each kidney. The tissue was processed and paraffin-embedded sections stained with hematoxylin and eosin (H&E) were examined. Acute pyelonephritis was characterized by the presence of intratubular neutrophils and interstitial infiltrates of mononuclear cells and neutrophils in the renal cortex (Fig. 1). The severity of inflammation was graded on the basis of the extent of involvement of the cortex present in the section as follows:

- Grade 1 = inflammation limited to ≤33% of the cortical area.
- Grade 2 = inflammation involving between 34% and 67% of the cortical area.
- Grade 3 = inflammation involving >67% of the cortical area.

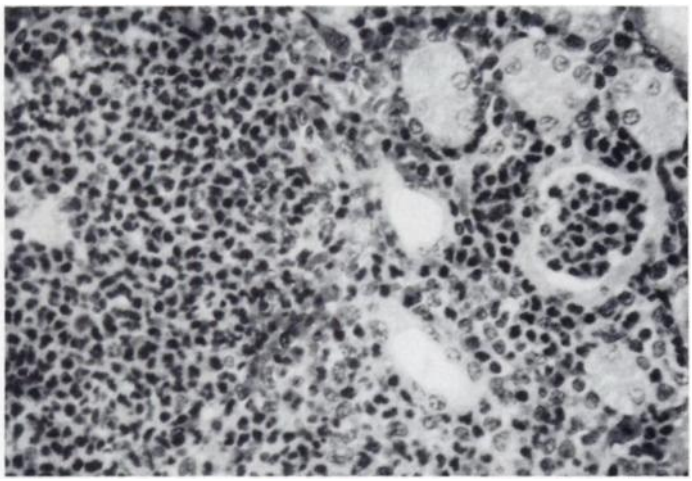

**FIGURE 1.** Acute pyelonephritis is characterized by the presence of neutrophils in the interstitium and in the lumen of a dilated tubule (mag. 400x. H&E).

### Interpreting and Processing the Images

Using a blinded coding system, the planar and SPECT images were interpreted independently at a later date without the knowledge of pathologic findings.

Interpretation of the planar images was based on the evaluation of digital images on the computer monitor. The criteria for acute pyelonephritis on planar images was the presence of focal, multifocal or diffuse decreased cortical uptake of DMSA (Fig. 2A,B and 3A,B).

SPECT images were reconstructed on 64 × 64 matrix without attenuation correction, using a Ramp filter with a cutoff frequency of 0.9 cycles/cm. The coronal, sagittal and transverse images were first viewed without reorientation. Each kidney was then reconstructed separately after rotating the images to obtain true anatomic sagittal, coronal and transverse slices. The SPECT criteria for the diagnosis of acute pyelonephritis was subjective evidence of focal area(s) of decreased uptake seen at least on two projections. No attempt was made to quantify the severity of decreased uptake (Figs. 2C and 3C).

Images of each kidney were classified as positive or negative for acute pyelonephritis regardless of the severity and number of lesions.

To evaluate the accuracy of SPECT and pinhole imaging for the detection of individual pyelonephritic lesions, each kidney was arbitrarily divided into three zones (upper, middle, lower). Image

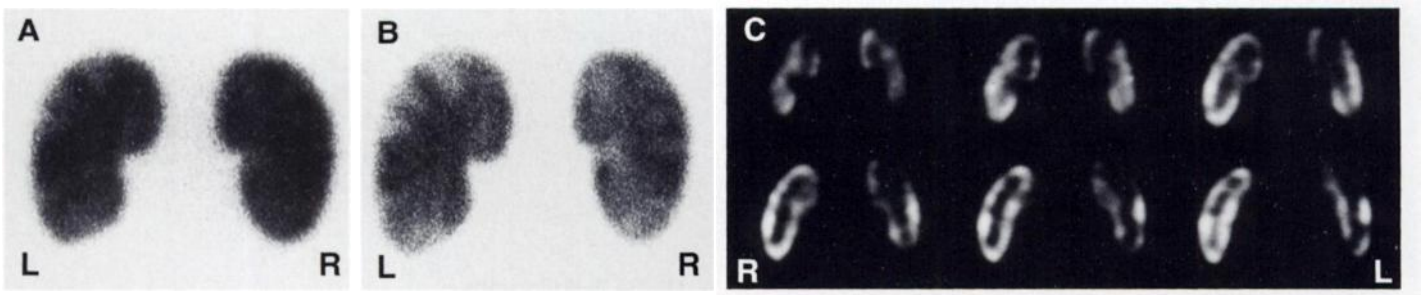


**FIGURE 2.** Bilateral multifocal pyelonephritis demonstrated on both pinhole and SPECT images. (A) Planar image using parallel-hole collimation shows multiple areas of decreased $^{99m}$Tc-DMSA uptake along the lateral aspect and in the lower pole of the left kidney. There is also a suggestion of a small lesion in the lateral aspect of the right kidney. (B) Magnified posterior pinhole images of the kidneys clearly show multiple lesions in both kidneys. (C) Coronal SPECT images demonstrate bilateral lesions.

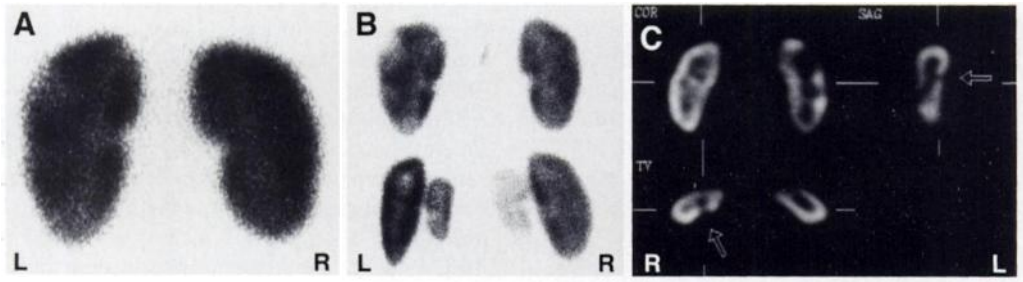


**FIGURE 3.** Multifocal acute pyelonephritis of the left kidney is clearly seen on both parallel-hole (A) and pinhole (B) images. A small lesion in the posterior aspect of the right kidney (arrows) was seen only on the SPECT (C).

**TABLE 2**
Pathologic and Scintigraphic Findings in 32 Kidneys Exposed to Infected Urine for 1-10 Days

| | Pinhole | | SPECT | |
|---|---|---|---|---|
| Pathology | Pos. | Neg. | Pos. | Neg. |
| Postive (*24*) | 20 | 4* | 22 | 2* |
| Negative (*8*) | 0 | 8 | 2 | 6 |
| Sensitivity | 83% | | 92% | |
| Overall accuracy | 88% | | 88% | |

*Two were the same kidneys. Pos. = positive; Neg. = negative

findings were then compared with the pathology results for the presence or absence of acute pyelonephritis in each zone.

## RESULTS

Histopathology showed evidence of a single or multiple foci of acute pyelonephritis in 24 kidneys (58 renal zones) of 15 piglets (9 bilateral; 6 unilateral). Extensive multifocal acute pyelonephritis was documented in all 6 kidneys (18/18 zones) which had been exposed to infected urine for 10 days. Less severe lesions were seen in 5 of 8 kidneys (13/24 zones) and 9 of 10 kidneys (20/30 zones) which had been exposed to infected urine for 3 and 2 days, respectively. Mild lesions were also seen in 4 of 8 kidneys (7/24 zones) which had been exposed to infected urine for $\leq$ 24 hr (Table 1).

### Detection of Affected Kidneys

Acute pyelonephritis was correctly diagnosed on the pinhole images in 20 of 24 affected kidneys for a sensitivity of 83%. There were no false-positive results. The SPECT images correctly demonstrated evidence of acute pyelonephritis in 22 of 24 affected kidneys for a sensitivity of 92%. Acute pyelonephritis was missed on both SPECT and pinhole images in two kidneys and on pinhole images in only another two. In each of these four kidneys, a single pyelonephritic lesion was found and all were of grade I in severity. The SPECT images, however, were interpreted as abnormal in two of eight kidneys with no pathologic evidence of acute pyelonephritis (false-positive). Since there were only eight kidneys without histopathologic evidence of acute pyelonephritis, calculation of the specificity of these techniques for the detection of affected kidney was not meaningful. Overall agreement with pathology for the presence or absence of pyelonephritis was 88% for both imaging techniques (Table 2).

If the eight kidneys exposed to infected urine $\leq$ 24 hr were excluded, there were two false-negative results, one with pinhole only and one with both pinhole and SPECT. In this subgroup there were no false-positive results with either technique (Table 3).

**TABLE 3**
Pathologic and Image Findings in 24 Kidneys Exposed to Infected Urine for 2-10 Days

| | Pinhole | | SPECT | |
|---|---|---|---|---|
| Pathology | Pos. | Neg. | Pos. | Neg. |
| Positive (*20*) | 18 | 2* | 19 | 1* |
| Negative (*4*) | 0 | 4 | 0 | 4 |
| Sensitivity | 90% | | 95% | |
| Overall accuracy | 92% | | 96% | |

*One was the same kidney. Pos. = positive; Neg. = negative

**TABLE 4**
Pathologic and Scintigraphic Findings in 96 Renal Zones Exposed to Infected Urine for 1-10 Days

| | Pinhole | | SPECT | |
|---|---|---|---|---|
| Pathology | Pos. | Neg. | Pos. | Neg. |
| Positive (*58*) | 50 | 8* | 53 | 5* |
| Negative (*38*) | 2 | 36 | 7 | 31 |
| Sensitivity | 86% | | 91% | |
| Specificity | 95% | | 82% | |
| Overall accuracy | 90% | | 88% | |

*Three were the same zones. Pos. = positive; Neg. = negative

### Detection of Affected Zones

Considering all 96 zones (32 kidneys), acute pyelonephritis was documented histologically in 58 of 96 zones. Of 58 affected zones, 50 were demonstrated on the pinhole images and 53 on the SPECT images. Five zones were false-negative on only the pinhole images (four grade I; one grade II), two on SPECT (one grade I; one grade II) and three on both (all grade I). There were two false-positive zones with pinhole images which were also falsely positive on SPECT. There were additional five false-positive zones with SPECT for a total of seven zones (Table 4).

Excluding the eight kidneys that were exposed to infected urine $\leq$ 24 hr, acute pyelonephritis was histologically documented in 51 of 72 zones. Of 51 abnormal zones, 46 were seen on pinhole images and 49 on SPECT. Acute pyelonephritis was missed in five zones, three on pinhole images only (two grade I; one grade II) and two on both pinhole and SPECT images (both grade I). There was one false-positive zone with both SPECT and pinhole (Table 5).

## DISCUSSION

In a previous experimental study we induced unilateral reflux of infected urine in 29 piglets and obtained planar DMSA scans using converging collimator at 1 or 2 wk after the introduction of bacteria into the bladder. We found planar DMSA scans using a converging collimator to be 87% sensitive and 97% specific for the detection of acute pyelonephritis in piglets (*1*). Subsequently, Parkhouse et al., using a similar experimental model, reported a sensitivity of 89% and specificity of 100% for planar DMSA scan (*2*). These experimental studies proved that planar DMSA scintigraphy is a highly sensitive and reliable technique for the detection of acute pyelonephritis in piglets. Because of the close similarity between porcine and human kidneys, there is every reason to believe that the same degree of accuracy can be obtained in the diagnosis of acute pyelonephritis in humans.

**TABLE 5**
Pathologic and Image Findings in 72 Renal Zones Exposed to Infected Urine for 2-10 Days

| | Pinhole | | SPECT | |
|---|---|---|---|---|
| Pathology | Pos. | Neg. | Pos. | Neg. |
| Positive (*51*) | 46 | 5* | 49 | 2* |
| Negative (*21*) | 1 | 20 | 1 | 20 |
| Sensitivity | 90% | | 96% | |
| Specificity | 95% | | 95% | |
| Overall accuracy | 92% | | 96% | |

*Two were the same zones. Pos. = positive; Neg. = negative

Clinical studies comparing SPECT and planar (with or without pinhole collimator) techniques in children have been reported to show SPECT to be significantly more sensitive than planar imaging, based on the detection of a greater number of cortical "defects" (*3,4*). Tarkington et al., using a state of the art multidetector SPECT camera, compared SPECT and pinhole techniques in 33 children with a variety of renal disorders including urinary tract infection. They found "enhanced" diagnostic information with SPECT in 71% of the kidneys. More important, they reported detection of cortical "defects" by SPECT in 15 of 24 (63%) kidneys that appeared normal on pinhole scan (*3*). The nature and significance of the "cortical defects" which were seen on SPECT and not seen on pinhole images were unknown. To corroborate their impression of the increased accuracy of SPECT imaging, they subsequently evaluated the accuracy of SPECT DMSA for the detection of experimental acute pyelonephritis in piglets and reported a sensitivity of 97% and specificity of 93% (*5*). Unfortunately, in their experimental study, they did not compare SPECT with pinhole imaging.

In our previous study, scans were obtained after 7 or 14 days of exposure to infected urine. In contrast, the duration of exposure of the kidneys to infected urine in the present study varied from 1 to 10 days. Therefore, we were able to evaluate pyelonephritic lesions in different stages of development and with varying degrees of severity. Eight of 32 kidneys were exposed to infected urine for 1 day only, 18 for 2–3 days and 6 for 10 days (Table 1).

For all 32 kidneys, the sensitivity of SPECT for the detection of affected kidneys appears to be superior to pinhole imaging (92% versus 83%), but the overall accuracy was 88% for both (Table 2). SPECT results for eight kidneys exposed to infected urine for 24 hr were two false-positives and one of two false-negatives; pinhole imaging resulted in four false-negatives. Both false-positive results on SPECT were manifested as a single small area of decreased uptake not different from some other subtle defects which proved to be true-positive. The pinhole images of these two kidneys were normal. A solitary lesion in one of these eight kidneys was missed on both SPECT and pinhole images, but the lesion in another kidney was missed only on the planar images.

To better mimic the clinical situation where patients would not likely be evaluated within 24 hr of acquiring infection, we excluded the eight kidneys with 24-hr exposure to infected urine in a separate analysis. In this subgroup, there were two false-negatives with pinhole, one false-negative with SPECT and no false-positives with either technique. Therefore, the difference in sensitivity of SPECT and pinhole for the detection of pyelonephritis in kidneys exposed to infected urine longer than 1 day becomes even less significant (95% versus 90%) (Table 3).

For all 96 renal zones (32 kidneys), the sensitivity of SPECT for the detection of affected renal zones was slightly better than pinhole imaging (91% compared with 86%), but its specificity was lower (82% compared with 95%) resulting in a similar overall accuracy for both techniques. Again, excluding the eight kidneys exposed to infected urine for 24 hr, the sensitivity of SPECT for detecting involved renal zones was slightly better than pinhole imaging (96% compared with 90%), but the specificity was similar for both techniques, resulting in slightly higher accuracy for SPECT (96% compared with 92%).

Planar imaging using pinhole magnification, while dependent on careful positioning, does not require further technical intervention for the display of the images. In contrast, the production of SPECT images involves meticulous attention both to acquisition as well as processing of the data. SPECT results can be radically influenced by the choice of filter. Normal heterogeneity of uptake within the renal cortex can mimic areas of abnormally decreased uptake. Therefore, the higher sensitivity of SPECT imaging in detecting small cortical lesions is achieved at the expense of a correspondingly lower specificity. While the scanning time is approximately the same for both planar and SPECT imaging, the patient must remain still throughout the entire SPECT acquisition. Small movements at any point necessitate beginning the study over again. On the other hand, if a patient moves while a pinhole image is being obtained, it is more easily repeated. Thus, for young children, sedation may be required more often for SPECT compared to planar imaging.

## CONCLUSION

This study corroborates the high sensitivity of planar imaging previously found in the experimental studies by us and others. Although the sensitivity of SPECT is slightly better than planar (pinhole) DMSA scan, the overall accuracy of these two imaging techniques is essentially the same.

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