**J of Nuclear Medicine Technology, first published online April 13, 2017 as doi:10.2967/jnmt.117.192401**

# CHANGING USE PATTERNS FOR $^{99m}$TC MAA FROM 2000 TO 2015

James A Ponto, MS

Chief Nuclear Pharmacist, University of Iowa Hospitals and Clinics, and Clinical Professor, University of Iowa College of Pharmacy

Funding support: none

Acknowledgements: none

Previous presentation: Contributed Paper Poster at the American Pharmacists Association (APhA) Annual Meeting and Exposition in San Francisco, CA, March 24-27, 2017

Correspondence/reprints: James A Ponto, MS, BCNP

Nuclear Medicine 3832 JPP

University of Iowa Hospitals and Clinics

Iowa City, IA 52242

Phone: 319-356-2741

Fax: 319-384-6389

Email: james-ponto@uiowa.edu

Word count: 1686

Conflicts of Interest: The Author has no conflicts of interest – either financial or otherwise – that may directly or indirectly influence the content of the submitted manuscript.

running title: $^{99m}$Tc MAA Changing Use Patterns

ABSTRACT

Since the early 2000's, evaluation of pulmonary embolism (PE) has shifted from $^{99m}$Tc macroaggregated albumin (MAA) perfusion lung scans to CT angiography (CTA). $^{99m}$Tc MAA continues to be used in patients with contraindications to CTA and for other uses. A reduced number of MAA particles is used in patients with pulmonary hypertension (PH) or other risk factors. This study assessed the changing use patterns for $^{99m}$Tc MAA by comparing snap-shots of procedures in 2000 and in 2015 in one institution.

Methods:

Records for all patients receiving $^{99m}$Tc MAA in the year 2000 and in 2015 were reviewed, making note of the imaging procedure, any contraindication to CTA, and if a reduced number of MAA particles was used.

Results:

In 2000, $^{99m}$Tc MAA was used for 489 lung scans for PE, 2 peritoneovenous shunts, and 1 cardiac shunt. Of the lung scan patients, 46 (9%) had PH. A reduced number of particles was used for PH and cardiac shunt patients, 47/492 = 9%.

In 2015, $^{99m}$Tc MAA was used for 263 lung scans for PE, 33 pre-surgical planning scans, 33 lung transplants, 16 pulmonary artery stenosis, 5 hepatic artery microspheres eligibility, and 1 peritoneovenous shunt. Of the lung scans for PE, 256/263 (97%) had a contraindication to CTA or a non-diagnostic CTA, including 99 (38%) with PH. A reduced number of particles was used for PH, pre-surgical, and lung transplant patients, 165/351 = 47%.

Conclusion:

Comparing 2015 to 2000, lung scans for PE decreased 46% from 489 to 263, apparently due to CTA, while other uses rose from 3 to 88. Use of reduced number of particles rose significantly from 9% to 47% of $^{99m}$Tc MAA doses. Although the total number of $^{99m}$Tc MAA doses dropped 29% from 492 to 351, $^{99m}$Tc MAA remains an important radiopharmaceutical for both PE and other uses.

KEY WORDS: $^{99m}$Tc MAA; lung scans; MAA particles; macroaggregated albumin

## INTRODUCTION

Since its introduction in the mid-1960's, $^{99m}$Tc albumin aggregated (commonly known as macro-aggregated albumin; MAA) has served for decades as a valuable radiopharmaceutical in the evaluation of lung perfusion. Especially when coupled with radioactive gas or radioaerosol airway imaging, ventilation/perfusion (V/Q) lung scans have been a mainstay in the evaluation of pulmonary embolism.(*1*) With the development of spiral CT in the mid-1990's and its widespread adoption in the early 2000's, there has been a dramatic shift from V/Q lung scans to CT angiography (CTA) for evaluation of pulmonary embolism (PE).(*1*) However, $^{99m}$Tc MAA has continued to be used for V/Q scans, especially for patients with contraindications to CTA (*1,2*) and has found utility in a variety of other uses such as evaluation of pulmonary artery stenosis, lung transplants, presurgical planning, and eligibility for $^{90}$Y microspheres intravascular brachytherapy.(*3-5*)

Severe pulmonary hypertension is a labeled contraindication for using $^{99m}$Tc MAA, and right-to-left cardiac shunting is listed as a precaution.(*6*) In these situations, professional practice guidelines recommend administering a reduced number of particles.(*3,5*)

The objective of this study was to assess the changing use patterns for $^{99m}$Tc MAA by comparing snap-shots of procedures in 2000 and in 2015 in one institution.

## MATERIALS AND METHODS

Medical records for all patients receiving $^{99m}$Tc MAA in the calendar years 2000 and 2015 were reviewed. This project was submitted to the IRB, and the IRB chair determined this study did not require IRB review and accordingly did not require informed consent. Notes were made of the imaging procedure, any contraindication to CTA, and whether a reduced number of MAA particles was ordered. Results were tabulated for each year. A two proportion z test (alpha = 0.05) was used to evaluate whether or not there were statistically significant changes in the fraction of patients receiving a reduced number of MAA particles.

## RESULTS

The uses of $^{99m}$Tc MAA and their respective frequencies for the years 2000 and 2015 are detailed in Table 1.

In 2000, 46/489 (9.4%) of the V/Q patients received a reduced number MAA particles because of pulmonary hypertension. A reduced number of particles was also used for the cardiac shunt patient, resulting in the total number of patients receiving a reduced number of MAA particles of 47/492 (9.6%).

In 2015, 99/263 (37.6%) of the VQ patients received a reduced number of MAA particles because of pulmonary hypertension. A reduced number of particles was also used for pre-surgical and lung transplants patients, resulting in the total number of patients receiving a reduced number of MAA particles of 165/351 (47.0%).

Statistical analyses using two proportion z tests showed statistically significant increases in the fraction of patients receiving a reduced number of MAA particles for V/Q scans ($z = 9.4$, $p < 0.01$) and in the fraction of all patients receiving a reduced number of MAA particles for any reason ($z=10.7$, $p < 0.01$) in 2015.

As shown in Table 1, the number of V/Q scans substantially decreased from 2000 to 2015, presumably because of a shift to CTA. Of the V/Q scans that were performed in 2015, the vast majority of patients had a contraindication to CTA (see Table 2.)

Examination of Table 1 also reveals an increase in the variety and number of other uses of $^{99m}$Tc MAA in 2015 compared to 2000.

## DISCUSSION

FDA-approved indications for $^{99m}$Tc MAA are for the evaluation of lung perfusion and for peritoneovenous (LeVeen) shunt patency.(*6*) Although an off-label use, $^{99m}$Tc MAA imaging following hepatic artery injection is described as an eligibility test prior to treatment of liver tumors with $^{90}$Y microspheres.(*7,8*)

The recommended particle dose for $^{99m}$Tc MAA in adults is 200,000 – 700,000 with the suggested number being 350,000 particles.(*6*) Severe pulmonary hypertension is a specific contraindication for $^{99m}$Tc MAA.(*6*) However, a V/Q lung scan is considered a pivotal test in the definitive diagnosis and baseline characterization of pulmonary hypertension.(*9*) Hence, V/Q scans are routinely performed in patients with suspected or known pulmonary hypertension. In

these patients, professional practice guidelines recommend using a reduced number of particles, such as 100,000 – 200,000(*3*) or 100,000 – 150,000.(*5*) Doses with a reduced number of particles are also used in patients with right-to-left cardiac shunts,(*3*) lung transplants,(*10*) and pre-lung surgery scans (unpublished, institutional policy). Such doses with reduced number of particles generally require preparation of $^{99m}$Tc MAA outside of package insert instructions.(*11,12*) In 2000, doses with reduced number of particles were relatively rare (9%), but have become much more frequent in 2015 (47%).

Although CTA has replaced V/Q scans to a large extent, V/Q scans remain an important option for those patients who have a non-diagnostic CTA or have relative contraindications to CTA. Examples include patients with kidney disease/impaired renal function (e.g., chronic renal insufficiency or acute kidney injury), contrast allergy/previous reaction to contrast media, pregnancy, metformin therapy not interrupted, intravascular hypovolemia, pulmonary hypertension, and heart transplant rejection.(*2,13*) In 2015, 97% of our V/Q patients had a relative contraindication to CTA or a non-diagnostic CTA (see Table 2).

Data on $^{99m}$Tc MAA use were limited to snapshots of the years 2000 and 2015 in one institution. Results cannot be extrapolated to other institutions. Nonetheless, literature articles and professional practice guidelines suggest that the $^{99m}$Tc MAA lung scan remains an important, albeit less frequently performed, diagnostic test for pulmonary embolism, especially if the patient has a contraindication to radiopaque contrast media. Moreover, there appears to be a growing number of other uses.

## CONCLUSION

Comparing 2015 to 2000, the number of $^{99m}$Tc MAA lung scans for PE dropped from 489 to 263 (46% decrease), apparently due to CTA, while other uses rose in number from 3 to 88. Use of reduced number of particles rose significantly from 9% of doses to 47% of doses. Although the total number of $^{99m}$Tc MAA doses dropped from 492 to 351 (29% decrease), $^{99m}$Tc MAA remains an important radiopharmaceutical for PE and other uses.

REFERENCES

1. Yazdani M, Lau CT, Lempel JK, et al. Historical evolution of imaging techniques for the evaluation of pulmonary embolism. *RadioGraphics*. 2015;35:1245-1262.

2. ACR Committee on Drugs and Contrast Media. *ACR Manual on Contrast Media, Version 10.1.* Reston, VA. American College of Radiology; 2015.

3. Parker JA, Coleman RE, Grady E, et al. SNM practice guideline for lung scintigraphy 4.0. *J Nucl Med Technol*. 2012;40:57-65.

4. Gandhi SJ, Babu S, Subramanyam P, et al. Tc-99m macro aggregated albumin scintigraphy – indications other than pulmonary embolism: A pictorial essay. *Indian J Nucl Med.* 2013;28(3):152-162.

5. ACR-SNM-SPR practice parameter for the performance of pulmonary scintigraphy in adults and children. Revised 2014. http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/Pulmonary_Scintigraphy.pdf. Accessed September 14, 2016.

6. MAA package insert. Kirkland, Quebec, CA. DRAXIMAGE; 2002.

7. SIR-Spheres package insert. Wilmington, MA. Sirtex Medical; 2006.

8. TheraSphere package insert. Farnham, Surrey, UK. Biocompatibles; 2014.

9. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension: A report of the American College of Cardiology Foundation Task

Force on Expert Consensus Documents and the American Heart Association. *Circulation*. 2009;119:2250-2294.

10. Ponto JA. Radiopharmaceutical considerations for using Tc-99m MAA in lung transplant patients. *J Am Pharm Assoc*. 2010;50:419-423.

11. Levine EK, Perritt JS, Gordon L. Particle reduction of a macroaggregated albumin kit: simplified calculations. *J Nucl Med Technol*. 1989;17:143-144.

12. Bolstad DM, Valley TB, Wilson ME, Hung JC. An improved technique for reducing the number of particles in a technetium-99m macroaggregated albumin injection. *J Nucl Med Technol*. 1992;20:220-223.

13. Sadigh G, Kelly AM, Cronin P. Challenges, controversies, and hot topics in pulmonary embolism imaging. *AJR*. 2011;196:497-515.

TABLE 1. $^{99m}$Tc MAA Uses in 2000 and in 2015.

| Use | 2000 Number (%) | 2015 Number (%) |
|---|---|---|
| V/Q scan, routine number of particles | 443 (90.0%) | 164 (46.7%) |
| V/Q scas, reduced number of particles | 46 (9.3%) | 99 (28.2%) |
| Peritoneal-venous shunt patency | 2 (0.4%) | 1 (0.3%) |
| Right-to-left cardiac shunt | 1 (0.2%) | |
| Pulmonary artery stenosis | | 16 (4.6%) |
| Pre-surgical evaluation | | 33 (9.4%) |
| Lung transplant | | 33 (9.4%) |
| Hepatic artery microspheres eligibility | | 5 (4.6% |
| TOTAL USES | 492 (100%) | 351 (100%) |

TABLE 2. Contraindications to CTA in Patients Undergoing V/Q Scans in 2015

| Contraindication | Number (%) |
|---|---|
| None | 7 (2.7%) |
| Acute kidney injury or chronic kidney disease | 121 (46.0%) |
| Contrast allergy | 18 (6.8%) |
| Pregnancy | 6 (2.3%) |
| Metformin therapy not stopped | 2 (0.8%) |
| Intravascular hypovolemia | 1 (0.4%) |
| Pulmonary hypertension | 99 (37.6%) |
| Heart transplant | 2 (0.8%) |
| Non-diagnostic CTA | 7 (2.7%) |
| TOTAL | 263 (100%) |