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Re: Positron Emission Tomography (N-13 Ammonia) for Myocardial Perfusion (#CAG-00165N)

The American Society of Nuclear Cardiology (ASNC) is a professional medical society which provides its members with a variety of continuing medical education programs related to Nuclear Cardiology, develops standards and guidelines for training and practice, promotes accreditation and certification in this sub-specialty field, and is the principal advocacy voice for Nuclear Cardiology. ASNC, now comprising over 4,500 members, is dedicated to high quality performance and appropriate utilization of nuclear cardiology testing to optimize the care of patients with known or suspected heart disease.

The American College of Cardiology (ACC) is a 29,000 member non-profit professional medical society and teaching institution whose purpose is to foster optimal cardiovascular care and disease prevention through professional education, promotion of research, and leadership in the development of standards and formulation of health care policy. The College represents more than 90 percent of the cardiologists practicing in the United States.

ASNC and the ACC appreciate the opportunity to provide our support for coverage of positron emission tomography (N-13 Ammonia) for myocardial perfusion imaging.

We strongly support Medicare coverage for the provision of services related to N13-ammonia for radionuclide imaging of myocardial blood flow using positron emission tomography (PET). This well validated tracer of myocardial blood flow has been studied for over 20 years, and data strongly support the use of this isotope for detecting or ruling out coronary artery disease (CAD) as well as its use in conjunction with FDG for assessment of myocardial viability. For the latter clinical application of imaging, CMS has approved reimbursement for FDG for that purpose on the basis of a pooled analysis of information in the literature. ASNC and the ACC believe that a similar pooled analysis of data also support the use of N13-ammonia for use as a myocardial blood flow tracer, as outlined below.

Detection of CAD

Table 1 summarizes the pooled results from the literature on the sensitivity and the specificity for detecting or ruling out CAD using PET N13-ammonia analysis of myocardial blood flow. As can be

seen from the Table, the very strong data equal or exceed the performance characteristics of the already approved isotopes available for this purpose, including the single photon agents thallium-201 and the Tc-99m-based agents sestamibi and tetrofosmin, as well as the approved and reimbursed PET agent rubidium-82.

There are some technical advantages to PET imaging of myocardial blood flow with N-13 ammonia in comparison to rubidium-82, most importantly in the longer half-life, which allows higher quality images with better count statistics. This feature also allows the routine simultaneous acquisition of information on left ventricular function by using ECG-gated techniques, which is possible though more technically challenging with rubidium-82.

Thus, the performance characteristics which are equal or superior to currently available agents, as well as the potential technical advantage of N-13 ammonia over rubidium-82 for imaging myocardial blood flow, all suggest that this agent should be approved and reimbursed for this purpose.

Table 1 Sensitivity and Specificity of [13N] ammonia PET for Detection of CAD

Author	Sensitivity	Specificity	Patients
Gupta	94%	95%	48
Tamaki	98%	100%	51
Schelbert	97%	100%	32
Yonekura	97%	100%	60

Tamaki N, Yonekura Y, Senda M, et al. Value and limitation of stress thallium-201 single photon emission computed tomography: Comparison with nitrogen-13 ammonia positron tomography. *Journal of Nuclear Medicine* 1988; 29: 1181-1188.

Yonekura Y, Tamaki N, Senda M, et al. Detection of coronary artery disease with 13N-ammonia and high-resolution positron emission tomography. *American Heart Journal* 1987; 113(3):645-654.

Gupta NC, Esterbrooks D, Mohiuddin S, et al. Adenosine in myocardial perfusion imaging using positron emission tomography. *Am Heart J* 1991; 122:293-301.

Schelbert HR, Wisenberg G, Phelps ME, et al. Noninvasive assessment of coronary stenosis with myocardial perfusion imaging during pharmacologic coronary vasodilation. VI. Detection of coronary artery disease in human beings with intravenous N-13 ammonia and positron computed tomography. *Am J Cardiol* 1982; 49: 1197-1207.

Assessment of Myocardial Viability

Recently, CMS announced that the use of FDG for the purpose of assessing myocardial viability would be a reimbursable service. This was based in part on a pooled analysis of the literature suggesting very good performance characteristics for predicting recovery of regional dysfunction of the left ventricle after revascularization, as well as prediction of improved symptoms after revascularization.

However, when FDG is used for assessment of myocardial viability, it is always paired with an analysis of myocardial blood flow, to create the "mismatch" or "match" patterns which are the validated signs of viability or non-viability respectively. The previous approval of FDG for this purpose did not specify a particular blood flow tracer that would be reimbursed for use with FDG. Because of this, laboratories that use FDG for this purpose are limited in their choice of blood flow tracers to those that are approved or reimbursed. Table 2 is a pooled analysis of literature of the use of FDG in conjunction with N13-ammonia for assessing myocardial viability. The literature is strong, and indeed the use of N13-ammonia for this purpose is not only at least equivalent to the data using any other blood flow tracer, but has distinct potential advantage over pairing FDG with the single photon tracers (thallium201 or Tc99m-sestamibiltetrofosmin). The most important advantage problematic due to attenuation, leading to potential false positive finding of "mismatch". Due to the higher energy isotope characteristics as well as the more routine use of attenuation correction with N13-ammonia PET for assessment of myocardial blood flow, pairing of this isotope for the assessment of blood flow along with FDG for assessment of glucose metabolism in studying myocardial viability is advantageous. Based on the data in Table 2 we believe that the use of N13ammonia for this purpose is at least equivalent to and perhaps even superior to the use of the currently reimbursable blood flow tracers.

Table 2. Predictive Values for Functional Recovery After Revascularization Using Combined [13N] ammonia and FDG with PET

Author	N	LVE F	Unit of Recovery	Sensitivity % (Segs)	Specificity % (Segs)	PPV % (Segs)	NPV % (Segs)	Diagnostic Accuracy (%)
Tillisch	17	32±14	Seg	95 (35/37)	80 (24/30)	85 (35/41)	92 (24/26)	88 (59/67)
Tamaki	22	NR	Seg	78 (18/23)	78 (18/23)	78 (18/23)	78 (18/23)	78 (36/46)
Tamaki	11	NR	Seg	100 (40/40)	37 (6/16)	80 (40/50)	100 (0/6)	82 (46/56)
Vanoverschelde	12	55±7	Seg	100 (12/12)	--	100 (12/12)	--	100 (12/12)
Vom Dahl	37	34±10	Seg	66 (29/44)	77 (90/116)	53 (29/55)	86 (90/105)	74 (119/160)
Maes	20	48±9	REF	82 (9/11)	67 (6/9)	75 (9/12)	75 (6/8)	75 (15/20)
Grandin	25	49±11	Seg	88(15/17)	50 (4/8)	79 15/19)	67 (4/6)	76 (19/25)
Tamaki	43	41	Seg	88 (45/51)	82 (65/79)	76 45/59)	91 (65/71)	85 (110/130)
Baer	42	40±13	Seg	93 (167/180)	66 (126/191)	72 (167/232)	91 126/139)	79 (293/371)
mean±SD	253			83±17	68±15	78±12	80±18	79±12

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Abbreviations: Ref= reference; N= number of patients; LVEF= left ventricular ejection fraction; PPV= positive predictive value; NPV= negative predictive value; Segs= number of segments; Seg= improvement in segmental function; REF= improvement in regional ejection fraction; NR= not reported; FDG= fluoro-deoxyglucose; Mismatch= flow-metabolism mismatch; UI= uptake index *
Segmental data not reported

We appreciate the opportunity to comment on this coverage issue. ASNC and the ACC both strongly support the approval of N13-ammonia as a covered service by CMS of PET for myocardial viability.

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Sincerely,



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