# Incidence of Nephrogenic Systemic Fibrosis (NSF) in Dialysis Patients Receiving Either a Standard or a High-Relaxivity Gadolinium Chelate Contrast Agent: A Single Center Study

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**Purpose:**

To retrospectively determine the incidence of nephrogenic systemic fibrosis (NSF)[1] in dialysis patients administered a high relaxivity linear gadolinium chelate, gadobenate dimeglumine (MultiHance (MH), Bracco) and compare this incidence to the previously documented incidence of NSF related to use of a standard linear gadolinium chelate, gadodiamide (Omniscan (OM), GE Healthcare) at our center.

**Materials and Methods:**

Institutional review board approval was obtained for this HIPAA-compliant study at our university tertiary care center; the requirement for informed patient consent was waived. A total of three data bases (Dermatopathology, Radiology Information System, Nephrology Transplant Center) were cross-referenced for identification and evaluation of patients with severe renal disease treated with routine dialysis who had a MH enhanced MR study from 2/1/2007 to 6/24/2008. A diagnosis of NSF was dependent upon a diagnostic deep skin punch biopsy of a suspicious lesion identified on routine integumentary examination. The incidence of NSF in this group of patients was compared to a different population of dialysis patients who were imaged at our institution using intravenous OM from 10/2003 to 2/2007, as previously described[2]. As inclusion criteria all patients were on dialysis at the time of MR scan(s), all patients had dialysis within 1 day of the scan, and there was no less than a 6 months period of follow up observation. MR scan dates, per exam dose, and cumulative dose of contrast agent administered to each patient was determined using a standardized checklist. To determine if the rate of NSF cases is different between the two patient groups, we constructed 95% score-based confidence intervals for the proportion of NSF cases in each group of subjects. We used non-overlapping confidence intervals to test for a difference in the incidence proportion. Wilcoxon rank sum test was used to test the following null hypothoses: (1) that the median OM dose was equal in patients who did and did not develop NSF and (2) that the median OM dose was equal to the median MH dose.

**Results:**

During the study period, 603 dialysis patients received MH at a mean cumulative dose of 0.11 mmol/kg (0.05 - 0.35 mmol/kg) and no cases of NSF were identified, with an upper 95% confidence bound of 0.45%. Of 312 dialysis patients who received OM, 8 (2.6%) of these patients developed NSF, with a 95% confidence interval [1.30%, 4.98%] (Fig.1). The mean cumulative dose of OM was 0.16 mmol/kg (0.1 – 0.9 mmol/kg) for all patients, and 0.28 mmol/kg (0.1 – 0.8 mmol/kg) for the NSF patients (Fig.2). The median OM dose was not equal in patients who did and did not develop NSF (p= 0.0282), and was not equal to the median MH dose ($p = 7.68 \times 10^{-11}$).

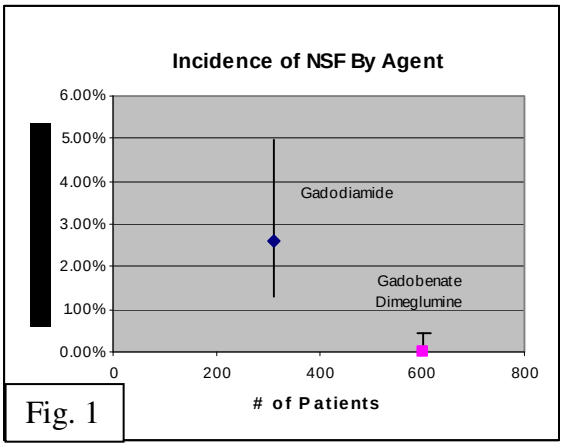


Fig. 1

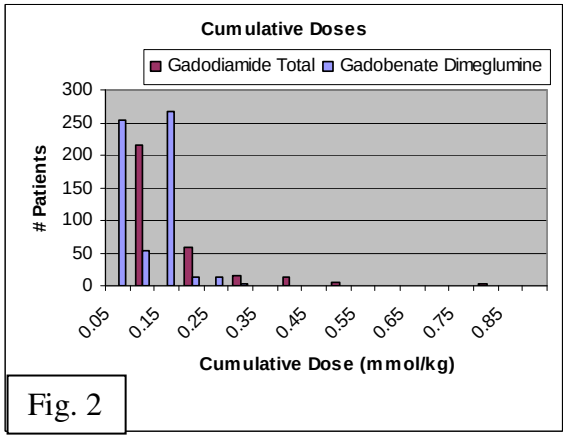


Fig. 2

**Conclusion:**

There was a statistically significant diminished incidence of NSF in dialysis patients at our center comparing patients who received a high relaxivity linear gadolinium chelate (MH) at a lower dose as compared to dialysis patients who received standard dose linear gadolinium chelate (OM).

**References:**

1. Cowper SE. Nephrogenic fibrosing dermopathy: the first 6 years. Curr Opin Rheumatol 2003;15:785–790.
2. Lauenstein TC, Salman K, Morreira R, Tata S, Tudorascu D, Baramidze G, Singh-Parker S, Martin DR. Nephrogenic systemic fibrosis: center case review. J Magn Reson Imaging 2007;26:1198–1203.
3. Grobner T. Gadolinium: a specific trigger for the development of nephrogenic fibrosing dermopathy and nephrogenic systemic fibrosis? Nephrol Dial Transplant 2006;21:1104–1108.
4. U.S. Food and Drug Administration. Public health advisory: gadolinium-containing contrast agents for magnetic resonance imaging (MRI): Omniscan, OptiMARK, Magnevist, ProHance, and MultiHance. U.S. Food and Drug Administration Web site. http://www.fda.gov/cder/drug/advisory/gadolinium_agents.htm. Published June 8, 2006. Updated May 23, 2007. Accessed November 19, 2007.
5. Thomsen HS; European Society of Urogenital Radiology (ESUR). ESUR guideline: gadolinium-based contrast media and nephrogenic systemic fibrosis. Eur Radiol 2007;17:2692–2696.
6. High WA, Ayers RA, Chandler J, Zito G, Cowper SE. Gadolinium is detectable within the tissues of patients with nephrogenic systemic fibrosis. J Am Acad Dermatol 2007;56:21–26.
7. Cowper SE. Nephrogenic fibrosing dermopathy: 2001–2007. International Center for Nephrogenic Fibrosing Dermopathy Research (ICNFDR) Web site. http://www.icnfdr.org. Accessed November 18, 2007.
8. Kanal E, Broome DR, Martin DR, Thomsen HS. Response to the FDA's May 23, 2007, nephrogenic systemic fibrosis update. Radiology 2007;246:11–14.
9. Collidge TA, Thompson PC, Mark PB, et al. Gadolinium-enhancing MR imaging and nephrogenic systemic fibrosis: retrospective study of a renal replacement therapy cohort. Radiology 2007;245:168–175.
10. Prince MR, Zhang H, Morris M, MacGregor JL, Grossman ME, Silberzweig J, DeLapaz RL, Lee HJ, Magro CM, Valeri AM. Incidence of nephrogenic systemic fibrosis at two large medical centers. Radiology 2008;248(3): 807-16.