GADOLINIUM RETENTION IN HUMANS: SURVEY OF RADIOLOGISTS AND IMPACT ON DAILY PRACTICE*

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ABSTRACT

Objective: We sought to assess the 1) awareness and impact of emerging gadolinium retention data on preferences of radiologists in their practice, and 2) factors that influence the attitudes about gadolinium use and risk. This study also documents various specifics of radiology practice in Turkey.

Methods: A twenty-one question survey was directed to radiologists who were at least one year from completion of residency and/or fellowship training. A survey link was emailed to the members of the Turkish Society of Radiology and was active for four weeks. The results were statistically analyzed.

Results: Three hundred and thirty-five radiologists completed the survey. At the time of this survey, 89% of respondents were aware of gadolinium retention in the brain. Forty-five percent of respondents said they decreased the amount of gadolinium administered and/or frequency of gadolinium-enhanced scans since the emergence of the gadolinium retention data. Eighty-eight percent of radiologists, who were aware of the molecular classification of different gadolinium agents, used a macrocyclic agent. Thirty-nine percent (n=130) had switched to a macrocyclic agent from a linear agent within the previous three years. Radiologists’ attitudes toward gadolinium retention were significantly associated with their background factors such as experience in radiology, subspecialty training, and daily work definition, amongst others. Observation of hyperintense dentate nuclei due to gadolinium retention was uncommon in daily practice.

Conclusions: Gadolinium retention publications have affected the practice of contrast enhanced Magnetic resonance imaging (MRI) scans, mostly in the form of switching to a macrocyclic gadolinium agent and decreasing utilization of gadolinium in general for some scans, mostly in the form of switching to a macrocyclic gadolinium agent and decreasing utilization of gadolinium in general for some indications. These changes varied among radiologists by background factors.

Keywords: Gadolinium, magnetic resonance imaging, surveys and questionnaires, radiologists, cerebellar nuclei

ÖZET

Amaç: Bu çalışmada, 1) Son yıllarda ortaya konulan, insan beyninde gadolinium birkimi verileri hakkında radyologların farklındaki, klinik uygulamanın ve tercihleri üzerindeki etkisi ve 2) Gadolinium kullanımı ve riski hakkında yaklaşımları etkileyen faktörlerin değerlendirilmesi amaçlanmıştır. Ayrıca bu çalışmada, Türkiye’deki radyoloji pratikleri hakkında önemli bilgiler sunuldu.

Yöntem: İhtisas veya yan dal eğitimin tamamlanmasından en az bir yıl geçmiş olan radyologlara yönelik 21 soruluk anket hizmet etti. Türk Radyoloji Derneği üyesine e-posta ile gönderilen anket linki dört hafta boyunca aktifti.

Bulgular: Üç yüz otuz beş kişi anketi tamamladı. Katılımcıların %89’u beyinde gadolinium birkimi hakkında gelişmelerden haberdardı. Katılımcıların %45’i gadolinium birkimi verilerinin ortaya çıkmışından bu yana uyguladıkları gadolinium miktarını ve/veya gadolinium gerektiren görüntülemlerin sıfırlandırmamasını farkında olan radyologların %88’i makrosiklik bir ajan kullanmışdı. Yüzde 39’u (n=130) önceki üç yıl içinde (2015-2018) lineer bir ajanından makrosiklik bir ajan seçtiği bildirdi. Radyologların gadolinium birkimine yönelik yaklaşımları, radyoloji deneyimi, üst ihtisas eğitimi, kurum ve bilim radyoloji konferansına katılım süresi gibi kişye özel faktörelere önemli ölçüde ilişkilidi. Katılımcıların üç yüz on iki kişi gadolinium birkimindeki belirgin hiperintens nökteleri gözlemlemeye çalıştığı belirtilti.

Sonuç: Gadolinium birkimini davranışları, radyologların MR görüntüleme pratiklerini ve yaklaşımını, çoğunlukla makrosiklik gadolinium ajanlarına geçiş ve gadolinium kullanımı azaltmak suretiyle etkilemiştir. Bu değişiklikler, radyologların bireysel koşullarına göre değişiklik göstermektedir.

Anahtar Kelimeler: Gadolinium, manyetik rezonsan görüntüleme, anketler, radyoloji uzmanları, serebellar çekirdekler

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INTRODUCTION

Since the original reports of intracranial gadolinium retention/deposition in 2014, a number of studies have been published that attribute Hyperintense Dentate Nuclei (HDN) on T1-weighted MR images to repeated administrations of intravenous gadolinium (1-8). The clinical ramifications of gadolinium deposition have been debated and not yet substantiated, but the possible unwanted outcomes have worried practitioners, patients, drug companies and government organizations (9-11). On the other hand, while alternative contrast agents are being investigated, gadolinium is still integral to many Magnetic resonance imaging (MRI) protocols (12, 13). Involvement of radiologists in study ordering, appropriateness of scan indication, optimum protocoling and patient engagement are among the new areas of emphasis on utilization (14-16). Despite the numerous publications and significant research activity around the potential impact of gadolinium retention in the human body, little is known about the impact of these initiatives on daily radiology practice. Practice diversity exists across the globe. This study was based in Turkey, a country where the majority of radiologists individually prescribe gadolinium for their patients prior to MRI scans. Thus, their personal preferences may have a direct impact on the landscape of gadolinium utilization. This is important, as the study was conducted in a period when there was no limitation on the utilization of linear gadolinium molecules in the market yet. In this regard, the aim of this study was two-fold: 1) to assess the awareness and impact of emerging gadolinium retention data on the preferences of radiologists in their practice, and 2) analyze the factors that influence the attitudes about gadolinium use and risk.

METHODS

A survey was created using www.surveymonkey.com (San Mateo, CA) (see Appendix 1). The survey was anonymous with no personal information like name, sex, race, age or the name of the institution being asked, thus, as per ethical committee regulations, the study did not require IRB processing. All respondents read a written informed consent and agreed to participate prior to proceeding with the survey questions. Each question included a ‘no response’ choice to allow participants not to share their opinions. The survey was addressed to radiologists who were at least one year from completion of residency and/or fellowship training. A closed survey link was emailed to the members of the Turkish Society of Radiology and a reminder email was sent two weeks later. The survey was active during four weeks (October-November 2018). The survey was set to allow only one individual response per device, to prevent repetitive responses. A total of 21 multiple-choice questions were asked. Participants were able to skip any question. Statistical analyses were performed using SPSS version 21.0 for Windows (SPSS, Chicago, Ill). Descriptive statistics are presented. Decimals of percentages were rounded, as the actual numbers of samples (n) were provided. Respondents were grouped according to types of institution, scope of daily radiology practice, experience in radiology, and frequency of their attendance at radiology conferences/meetings. Normality of the variables’ dispersion was tested with the Kolmogorov-Smirnov test. Nonparametric Kruskal-Wallis H Test was used to test the difference between the groups, because all tested variables showed a non-Gaussian dispersion (p<0.0001 on Kolmogorov-Smirnov test for all variables). Groups were statistically analyzed and significant data for each subgroup are presented in a table (Table 1).

RESULTS

Three hundred and thirty-five members of Turkish Society of Radiology with at least one year of experience after radiology training completed the survey.

Background of respondents

Thirty-one percent (n=103/335) of respondents were affiliated with government-run community hospitals, 48% (n=160) with academic institutions, and 21% were affiliated with a private practice (n=64 private hospital; n=7 imaging centers). Seventy-two percent (n=242/335) of respondents defined their daily radiology practice as a general diagnostic radiology, 22% (n=72) as a diagnostic subspecialty, and 6% (n=21) as an interventional subspecialty. There was significant difference between participants’ daily work definition based on their institution. Most of the community hospitals and private practice radiologists (94% and 83%, respectively) were performing general radiology as opposed to academic center radiologists (53%, p=0.0001). 50% (n=167) of respondents were 1 to 5 years from their previous training period (either fellowship or residency), 19% (n=63) were 5 to 10 years, 10% (n=33) were 10 to 15 years, and 20% (n=67) were more than 15 years after their training period. Thirty-six percent (n=122) of respondents attended a radiology conference less frequently than once a year, 30% (n=101) attended once a year, and 30% (n=100) attended more frequently than once a year with 2% (n=5) attending conferences at least once a month. Forty-two percent of general radiology practitioners were attending a scientific conference less frequently than a year, as opposed to subspecialists and interventional radiologists (25% and 10%, respectively. p=0.02).

Awareness of radiologists and adoption in clinical practice

Twenty-two percent (n=84) did not know the class (macrocyclic or linear) of gadolinium agent they used. Twenty-six percent (n=86) were using a macrocyclic gadolinium...
Table 1. Grouped survey results with respect to background factors of respondents.

| Table 1. Grouped survey results with respect to background factors of respondents. | Daily work definition | Decision of gadolinium administration | Who prescribe gadolinium |
|---|---|---|---|
| | General diagnostic radiology | Interventional radiology | Subspeciality | p value | Radiologist prior to scan | Radiologist during the scan | Clinician | Radiologist and clinician’s collaboration | p value | Radiologist | Clinician | p value |
| Community hospital | 94% (n=97) | 2% (n=2) | 4% (n=4) | <.0001 | 11% (n=11) | 3% (n=3) | 74% (n=72) | 14% (n=14) | .021 | 8% (n=84) | 17% (n=17) | <.0001 |
| Academic centers | 53% (n=85) | 11% (n=17) | 37% (n=58) | 26% (n=41) | 7% (n=11) | 55% (n=88) | 12% (n=20) | 9.2% (n=147) | 7% (n=11) |
| Private practice | 83% (n=59) | 3% (n=2) | 14% (n=10) | 9% (n=6) | 35% (n=25) | 21% (n=15) | 35% (n=25) | 62% (n=44) | 35% (n=25) |
| Renal function tests prior to a gadolinium enhanced scan | | | | | | | | | |
| Not testing | eGFR | Serum creatinine level | Both creatinine and eGFR | Don’t know | p | Yes | No | p value | Yes | No | p value |
| Community hospital | 38% (n=39) | 6% (n=6) | 32% (n=33) | 12% (n=12) | 13% (n=13) | .003 | 31% (n=32) | 69% (n=71) | <.0001 | 59% (61) | 41% (n=42) | P<0.01 |
| Academic centers | 29% (n=47) | 6% (n=10) | 24% (n=39) | 29% (n=46) | 11% (n=18) | 38% (n=61) | 62% (n=99) | 5.5% (88) | 45% (n=72) |
| Private practice | 42% (n=30) | 10% (n=7) | 32% (n=23) | 14% (n=10) | 1% (n=1) | 61% (n=43) | 39% (n=28) | 75% (53) | 23% (n=16) |
| Frequency of HDN observation | | | | | | | | | |
| Never | Weekly | Monthly | Yearly | p value | 1-5 years | 5-10 years | 10-15 years | >15 years | p value | No | Yes | Don’t know | p value |
| Community hospital | 72% (n=74) | 2% (n=2) | 12% (n=12) | 11% (n=11) | .001 | 63% (n=65) | 21% (n=22) | 7% (n=7) | 8% (n=8) | <.0001 | 54% (n=56) | 25% (n=26) | 20% (n=21) | <.0001 |
| Academic centers | 65% (n=104) | 4% (n=7) | 13% (n=21) | 16% (n=26) | 51% (n=81) | 16% (n=26) | 11% (n=18) | 19% (n=31) | 22% (n=36) | 44% (n=70) | 34% (n=54) |
| Private practice | 47% (n=33) | 3% (n=2) | 21% (n=15) | 28% (n=20) | 2% (n=2) | 21% (n=15) | 11% (n=8) | 39% (n=28) | 41% (n=29) | 45% (n=32) | 14% (n=10) |
| Awareness of Gadolinium retention in human body | | | | | | | | | |
| Unaware | since 2015 | since 2016 | since 2017 | since 2018 | p value | Don’t know the class | Continues linear | Continues macrocyclic | To macrocyclic | To linear | p value |
| Community hospital | 14% (n=14) | 29% (n=30) | 28% (n=29) | 27% (n=28) | 2% (n=2) | .007 | 24% (n=25) | 7% (n=7) | 24% (n=25) | 39% (n=40) | 4% (n=4) | .001 |
| Academic centers | 4% (n=6) | 34% (n=55) | 36% (n=58) | 18% (n=28) | 8% (n=13) | 19% (n=31) | 6% (n=9) | 25% (n=40) | 45% (n=72) | 4% (n=6) |
| Private practice | 25% (n=18) | 30% (n=21) | 24% (n=17) | 18% (n=13) | 1% (n=1) | 39% (n=28) | 4% (n=3) | 30% (n=21) | 24% (n=17) | N/A |
| Decision of gadolinium administration | Radiologists involved in bulk purchase | Time passed since the previous residency or fellowship |
|---------------------------------------|---------------------------------------|------------------------------------------------------|
| Radiologist prior to scan | Radiologist during the scan | Clinician | Radiologist and clinician's collaboration | Yes | No | Don't know | p value | 1-5 years | 5-10 Years | 10-15 Years | >15 years | p value |
| General diagnostic radiology | 12% (n=28) | 10% (n=24) | 61% (n=147) | 17% (n=42) | p value | 43% (n=104) | 31% (n=76) | 26% (n=62) | .014 | 55% (n=132) | 19% (n=47) | 8% (n=19) | 16% (n=39) | .001 |
| Interventional radiology | 29% (n=6) | 10% (n=2) | 43% (n=9) | 19% (n=4) | | 33% (n=7) | 48% (n=10) | 19% (n=4) | | 52% (n=11) | 19% (n=4) | 5% (n=1) | 24% (n=5) |
| Subspeciality | 33% (n=24) | 18% (n=13) | 31% (n=22) | 18% (n=13) | | 15% (n=11) | 58% (n=42) | 26% (n=19) | | 33% (n=24) | 17% (n=12) | 18% (n=13) | 32% (n=23) |

| Awareness of gadolinium retention in human body | Frequency of attendance to radiology meeting/conferences |
|-----------------------------------------------|--------------------------------------------------------|
| General diagnostic radiology | Unaware | 12% (n=30) | 29% (n=70) | 30% (n=73) | 22% (n=54) | 6% (n=14) | p value | 1% (n=3) | 29% (n=71) | 24% (n=59) | 42% (n=102) | .02 |
| Interventional radiology | N/A | 24% (n=5) | 48% (n=10) | 29% (n=6) | N/A | | | | | | | |
| Subspeciality | 11% (n=8) | 44% (n=32) | 29% (n=21) | 13% (n=9) | 3% (n=2) | | | 3% (n=2) | 29% (n=21) | 43% (n=31) | 25% (n=18) |

| Timing of Gad agent switch | Type of institution |
|---------------------------|---------------------|
| Within previous three months | A year ago | 1-3 years ago | p value | Community hospital | Academic center | Private practice | p value |
| General diagnostic radiology | 12% (n=29) | 33% (n=79) | 12% (n=28) | .003 | 40% (n=97) | 35% (n=85) | 24% (n=59) | .015 |
| Interventional radiology | 5% (n=1) | 38% (n=8) | 24% (n=5) | | 10% (n=2) | 81% (n=17) | 10% (n=2) |
| Subspeciality | 8% (n=6) | 28% (n=20) | 32% (n=23) | | | | | |
### Table 1. Grouped survey results with respect to background factors of respondents. (Continued)

| Type of institution | General diagnostic radiology | Interventional radiology | Subspeciality | Radiologist prior to scan | Radiologist during the scan | Clinician | Radiologist and clinician’s collaboration | p value |
|---------------------|------------------------------|---------------------------|--------------|---------------------------|-----------------------------|-----------|------------------------------------------|---------|
| Community hospital  | 39% (n=65)                  | 77% (n=132)               | 7% (n=11)    | 15% (n=25)                | 7% (n=11)                   | 63% (n=105)| 15% (n=25)                              | <.0001  |
| Academic center     | 49% (n=81)                  | 75% (n=47)                | 6% (n=4)     | 13% (n=8)                 | 13% (n=8)                   | 57% (n=36)| 17% (n=11)                              | .001    |
| Private practice    | 12% (n=20)                  | 58% (n=19)                | 3% (n=1)     | 18% (n=6)                 | 9% (n=3)                    | 42% (n=14)| 30% (n=10)                              | .001    |
| >15 years from residency | 12% (n=8)            | 58% (n=37)                | 8% (n=5)     | 34% (n=23)                | 27% (n=18)                  | 7% (n=11) | 19% (n=13)                              | .033    |

| Daily work definition | Yes | No | p value |
|----------------------|-----|----|---------|
| General diagnostic radiology | 60% (n=3) | N/A |
| Interventional radiology | 40% (n=2) | <.0001 |
| Subspeciality | 80% (n=4) | 20% (n=1) | <.0001 |

| Details of gadolinium agent on MRI report | Never | Weekly | Monthly | Yearly | p value |
|------------------------------------------|-------|--------|---------|--------|---------|
| General diagnostic radiology | 68% (n=114) | 2% (n=3) | 13% (n=21) | 16% (n=27) | .022 |
| Interventional radiology | 70% (n=44) | 3% (n=2) | 11% (n=7) | 13% (n=8) | .001 |
| Subspeciality | 46% (n=15) | N/A | 24% (n=8) | 27% (n=9) | |

| Frequency of HDN observation | Never | Weekly | Monthly | Yearly | p value |
|------------------------------|-------|--------|---------|--------|---------|
| General diagnostic radiology | 68% (n=114) | 2% (n=3) | 13% (n=21) | 16% (n=27) | .022 |
| Interventional radiology | 70% (n=44) | 3% (n=2) | 11% (n=7) | 13% (n=8) | .001 |
| Subspeciality | 46% (n=15) | N/A | 24% (n=8) | 27% (n=9) | |

| Recently switching to a different class of gadolinium agent | Don't know the class | Continues linear | Continues macrocyclic | To macrocyclic | To linear | p value |
|------------------------------------------------------------|---------------------|------------------|-----------------------|----------------|----------|---------|
| General diagnostic radiology | 17% (n=17) | 7% (n=7) | 30% (n=30) | 42% (n=42) | 4% (n=4) | |
| Interventional radiology | 14% (n=14) | 6% (n=6) | 24% (n=24) | 53% (n=53) | 3% (n=3) | |
| Subspeciality | 41% (n=50) | 5% (n=6) | 22% (n=27) | 26% (n=32) | 3% (n=3) | |
agent and had not change it in the previous three years, 39% (n=130) were using a linear gadolinium agent and switched it to a macrocyclic agent in the previous three years, 6% (n=19) were still using linear gadolinium agents, 3% (n=10) were using a macrocyclic gadolinium agent and switched to a linear agent in the previous three years. In terms of the timing of change within the previous three-year period, 11% (n=36) switched to a gadolinium agent within the previous three months, 32% (n=107) in the previous year, 17% (n=56) within the previous three years. Thirty-six percent (n=107) switched because of gadolinium retention, 26% (n=77) because of NSF risk, and 11% (n=33) switched because of the agent's cost. In terms of gadolinium deposition, 11% (n=38) were unaware of emerging gadolinium retention data. This ratio was highest among those who attended a radiology conference less frequently than once a year (see Table 1 for details). Thirty-two percent (n=107) came to know of gadolinium deposition risk in 2015, 31% (n=104) in 2016, 21% (n=69) in 2017, and 5% (n=16) in 2018. Thirty-six percent (n=121) had not read the statements of the following organizations about gadolinium retention. Thirty-nine percent (n=132) read the American College of Radiology (ACR) and American Society of Neuroradiology (ASNR) statements, 7% (n=24) read the US Food and Drug Administration (FDA) statement, 15% (n=50) read the European Medicines Agency’s (EMA) pharmaceutical risk assessment committee statement on the matter. In terms of the impact of knowledge of gadolinium retention on practitioners’ clinical practice, 45% (n=152) said they decreased the amount and/or frequency of gadolinium-enhanced scans since the time that they found out about gadolinium deposition risk, while 46% (n=156) did not. Respondents were asked to rate the frequency of cases in which they faced diagnostic difficulty because of a reluctance to administer gadolinium. Twenty-two percent (n=73) answered ‘never’, 59% (n=195) answered ‘seldom’ and 19% (n=63) answered ‘frequently’. On the frequency of encountering HDN on pre-contrast MRI studies, 64% of radiologists (n=211) said ‘never’, 18% (n=58) said ‘once a year’, 15% (n=48) said ‘once a month’, 3% (n=11) said ‘once a week’. While 58% (n=54) respondents did report the existence of an HDN on their final MRI reports, 42% (n=39) did not. The highest HDN observation rates were seen in academic centers (Table 1). Forty-four percent (n=105) of respondents would include the generic name and amount of gadolinium agent used for a scan in their final MRI report, 56% (n=131) did not. One percent (n=3) of respondents faced a medico-legal problem or a complaint by patients and/or their relatives because of gadolinium administration, 99% (n=330) did not. All three of those who had a medico-legal problem were between 1-5 years from residency.

The rate at which radiologists detected HDN was highest among academic centers, followed by private practices and community hospitals, respectively (p<0.001, see Table 1. Grouped survey results with respect to background factors of respondents. (Continued)
Table 1 for details). Awareness of gadolinium retention was highest among academic centers and was followed by community hospitals and private practice (94%, 86% and 75% respectively, p=0.07, see Table 1 for details). Thirty-nine percent of private practice members were unaware of the class of gadolinium agent they were using as opposed to 24% in community hospitals and 19% in academic centers (p=0.001). Forty-five percent of academic centers switched from linear to macrocyclic agents and this was followed by community hospitals (39%) and private practices (24%, p=0.01). Unawareness rates of gadolinium deposition was inversely correlated with how frequently the physicians attended a radiology conference (22%, 7%, 2% and 0% in groups with; less frequent than once a year, once a year, more frequent than once a year and once a month, respectively. p<0.01)

Routine MRI workflow and protocolling
According to 53% (n=173) of respondents, the referring physician would decide whether to include post-gadolinium sequences for a given MRI scan. This practice was significantly common in community hospitals (Table 1). The remaining respondents said a radiologist would be involved in the decision-making process in the following roles: Prior to a particular scan, radiologist would decide whether gadolinium administration is needed (17%, n=58); At the time of a scan, after evaluating initial sequences (12%, n=29); and prior to a scan after a discussion with referring physician based on clinical indication (18%, n=59). The rate of a radiologist’s role in the decision-making process of gadolinium injection was the highest amongst interventional radiology practitioners. Interestingly, private practice radiologists had higher rates of involvement in gadolinium protocolling compared to academic centers and community hospitals (74% versus 55% and 21%, respectively p=0.021). For outpatient MRI scans, a radiologist would prescribe gadolinium in 84% (n=280), while the rest were prescribed by a referring physician (16%, n=55). Thirty-eight percent (n=128) of respondents were consulted in the hospital’s gadolinium purchase process for inpatient services, while 36% (n=122) were not. Twenty-five percent (n=85) said they were unaware of the hospital’s purchase process. Twenty-eight percent (n=95) of respondents were routinely testing serum creatinine levels before an MRI scan, 7% (n=23) tested eGFR levels and 20% (n=68) tested both creatinine and eGFR levels on a routine basis. Thirty-five percent (n=117) tested neither parameter and 10% (n=32) were unaware of renal function testing status prior to an MRI scan in their institution. Kidney function testing was highest in academic centers, followed by community hospitals and private practices (p=0.03, see Table 1 for details). Sixty percent (n=202) of participants offered agent specific (e.g. linear vs macrocyclic gadolinium) consent forms to patients prior to MRI scans, while 39% (n=131) did not. Forty-one percent (n=136) of participants recorded a cumulative dose of gadolinium administration from prior studies before undergoing an MRI scan, while 59% (n=199) did not. The rate of recording cumulative gadolinium administration from prior studies, including outside studies, was highest by radiologists in private practice (61% compared to 38% and 31% in academic centers and community hospitals, respectively p<0.0001). Agent specific consent acquisition was most common among private practice practitioners followed by community hospitals and academic centers (75%, 59% and 55%, respectively p<0.001).

DISCUSSION
Awareness of gadolinium retention has had a significant impact on practitioners’ approaches to contrast enhanced MRI scans, as nearly a half of our study participants decreased the amount of gadolinium administration per scan, and/or decreased the frequency of gadolinium-enhanced scans since they became aware of the gadolinium retention risk. This stance did not show any significant association with respondents’ background factors like institution, experience and practice type. Currently, the vast majority of participants in our present study use a macrocyclic agent, with more than half of them having switched to it within the previous three years (2015-2018), mostly during 2018. The rate of switching to a macrocyclic agent was highest among academic centers. This may be because they were the most concerned about gadolinium deposition, they were the heaviest users of linear agents prior to recognizing the gadolinium deposition controversy, or because of economic factors not explored by this study. Certainly the manufacturers of gadolinium agents have been marketing on the basis of reduced gadolinium deposition since the reports of HDN have arisen. In terms of reasoning, among those who switched to a different class of gadolinium, most stated they had done so because of recent gadolinium retention data, and this was followed by NSF risk and the agent’s cost. Moreover, despite several published studies in high impact journals (1-30), a tenth of radiologists are still unaware of gadolinium retention issues. This ratio was highest among those who attended a radiology conference less frequently than once a year. Frequency of attendance at a scientific conference was most common amongst interventional radiology practitioners. The awareness rate of gadolinium deposition was correlated with how frequently the radiologist attended a radiology conference. This signifies that despite the ubiquity of online and offline learning tools, conventional conferences are still an important source of practitioners’ update on HDN. On the other hand, observance of retained intracranial gadolinium is uncommon, as more than a half of our respondents had never noticed HDN in their daily practice, which maybe resultant of the scarcity of MRI utilization in their practice. The highest HDN observa-
Gadolinium retention and radiologists
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The present study also has critical findings in terms of radiology practice in Turkey. Participants in our study were affiliated with academic facilities, community hospitals, and private practices in decreasing order. Young radiologists were more commonly affiliated with community hospitals, possibly resulting from an ongoing Turkish government policy of obligatory duty in underserved areas after completion of a residency program. The majority of survey respondents defined their daily basis practice as general diagnostic radiology (low percentages of subspecialty focused practice). This is in line with the radiology training landscape reported by the European Society of Radiology (ESR), which showed fellowship training was not well established in European countries when compared with North America (26). Gadolinium retention data affected the majority of radiologists in this survey. Nonetheless, in the English literature, very few studies are available on impact of emerging gadolinium retention data on daily radiology practice and gadolinium enhanced MRI exercises (27-29). Despite diversity in adopted methods and their small sample sizes, available studies' overall results are in line with our present study. In their online open survey study conducted on Radiopedia.com, Fitzgerald et al. reported that 24 of 87 (28%) respondents made a change in their practice by either switching to a macrocyclic agent or decreasing the number of contrast enhanced MRI scans (29). This percentage is lower than our findings; however, their study was conducted at an earlier stage of gadolinium retention awareness. In an international survey study conducted on 58 neurosurgeons and neuroendocrinologists by Nachtigal et al., 28% of respondents were unaware of gadolinium retention risk (28). In their study 11% of respondents were unaware of the class of gadolinium agent they prescribed, a mildly lower rate than our findings (28). There is also a scarcity of studies focusing on contrast enhanced MRI exercises like gadolinium protocoling, consent forms, and renal function testing. In a study conducted on 162 pediatric radiologists (mostly academic centers from the USA), 25% of respondents would not contact the clinician and thus, the ordering physician would decide the MRI protocol as far as gadolinium administration (27). In our study this rate was significantly higher (53%). Together, our studies show that referring clinicians are deciding whether to administer contrast on MRI studies to a large extent. This may have caused unwarranted gadolinium injections (28).

More than a half of respondents in our study performed routine renal function testing prior to an enhanced MRI scan, mostly by testing serum creatinine levels. There was significant association between renal function testing and the type of institution. Academic centers had the highest renal function testing rates. In their aforementioned study, Blumfield et al. reported that 59% of their respondents required renal function testing only in selected cases (27). Two thirds of our respondents had distinct consent forms for each gadolinium class; same as the frequency of recording prior individual gadolinium administrations before undergoing an MRI scan. Prior exposure data recording was significantly higher among private practices and experienced radiologists. Recording prior administrations of gadolinium is important, as
Gadolinium retention has been shown to be dose-dependent (30).

In terms of reporting practices, more than a half of our respondents did not include the generic name and amount of gadolinium agent used for the scan in their final MRI report. Experienced radiologists had significantly higher reporting rates. More than half of those who encounter HDN would report this finding in their MRI report. Fitzgerald et al. reported that 38% of participants in their study had never seen HDN and 58% of their respondents would report HDN in the final MRI report, in line with our present findings.

The present study was conducted on a large cohort of radiologists from Turkey, thus the findings may not necessarily reflect the worldwide situation. However, findings of the current study were comparable to that of globally conducted studies (26, 28, 29). Because the name of institutions was not queried, the specific number of institutions participating in this study could not be quantified. Heterogeneity within the practice of a certain institution was not queried, as the study aimed to investigate the radiologists’ personal stance rather than institutional practices.

CONCLUSION

Gadolinium retention publications have affected radiologists’ preferences in the practice of contrast enhanced MRI scans, mostly in the form of switching to a macrocyclic gadolinium agent and decreasing utilization of gadolinium. These changes varied among radiologists by background factors such as experience in radiology, practice setting, and subspecialty training. Some of our findings about the practice of radiology in Turkey are potentially actionable. There may be a need for greater involvement of radiologists in study protocoling and gadolinium decision-making.

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Appendix 1: Survey questions.

This survey is designed solely for scientific research purposes and there is no financial relation with any company, institution or organization. The survey does not require any personal information. Please do not participate in the survey if one full year has not passed since your residency and/or fellowship training. To be part of this study, your current radiology practice should include MRI studies, please do not participate otherwise.

1-What kind of institution do you work for?

2-Which of the following best describes your daily radiology practice?

3-Who decides whether an MRI examination in your institution will be performed with or without IV contrast agent application?

4-If gadolinium is prescribed to patients before scan as part of your practice, who prescribes MR contrast agent in your hospital?

5- If contrast agents are provided by hospital itself, does hospital management consult radiologists before making bulk purchases of MRI contrast agent?

6-Do you routinely check kidney function before your patients are given gadolinium?

7-Do you question your patients’ exposure and amount of gadolinium before the contrast-enhanced MRI is performed?

8- Are you aware of molecular classes (linear or macrocyclic) of gadolinium agents? If so, have you changed the contrast agent you have prescribed in the previous three years?

9-If yes, why?

10- If yes, when did you change it?

11-How often do you attend to scientific conferences/meetings?

12- How many years ago did you complete your residency/fellowship training?

13-Have you heard that gadolinium accumulates in the brain after a certain amount of exposure in some individuals with a history of contrast-enhanced MRI scans? If so, when did you first get to know it? (Please jump to the 15th question if your answer to the first part of this question is No).

14-Did you change the amount or frequency of contrast agent application after being aware of gadolinium accumulation in the human brain?

15-Do you include in your MRI report the name and amount of contrast material given to the patient during scan?

16-Do you have a drug-specific consent form for the patients and/or relatives before administration of a contrast agent?

17- Have you ever observed a hyperintense dentate nucleus at your routine clinical MRI readings? If so how often do you observe?

18-Do you report hyperintense dentate nucleus in your MRI report?

19-Are you aware of the following medical institutions’ announces about gadolinium accumulation in the brain? (click all that apply).

20-Did you experience any diagnostic difficulties because you hesitated to use contrast media in your clinical practice?

21-Have you received any feedback from your patients about the accumulation of gadolinium in the brain or have you had any medical-legal problems?