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Magnetic Resonance Imaging for Patients with Brain Tumors During the COVID-19 Pandemic

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COVID-19; brain tumor; MRI; Imaging volume; Positivity rate

1. Abstract

1.1. Background and Purpose: The COVID-19 outbreak has posed unprecedented challenges for cancer imaging. The purpose of this study was to investigate the effect of the COVID-19 pandemic on brain tumor imaging.

1.2. Materials and Methods: We reviewed the database of adult brain tumors MR examinations with advanced MR perfusion imaging and diffusion tensor imaging, from March 15 to May 16, 2020. We investigated the imaging volume changes based on age, gender, reason of scan (New and Follow-up), and tumor subtypes. We calculated the "Negativity rate" and the "Positivity rate". In patients with glioma and brain metastasis, we evaluated the "Percentage of total increased abnormalities". We compared to the same period in 2019 using the Chi-Square test. We investigated the association between the latest results and prior imaging findings with Spearman's correlation.

1.3. Results: There were 250 advanced MRI examinations in 2020, 35.6% decline of imaging volume in 2019. The maximal weekly drop was in the second week (60%). The "Positivity rate" in 2020 (64.8%) was higher than in 2019 (57.7%, p=0.044). In the 205 advanced MRI examinations for patients with glioma and brain metastasis in 2020, the "Percentage of total increased abnormalities" was significantly higher than 2019. The latest imaging diagnosis of "Total increased abnormalities" and "stable" had significant association with their prior imaging findings, p<0.001.

1.4. Conclusion: Our study showed dramatic decline in the volume of advanced MRI of brain tumors during the first wave of COVID-19 pandemic compared to 2019, with significantly increased "Positivity rate" and "Percentage of total increased abnormalities".

2. Introduction

The coronavirus disease 2019 (COVID-19) pandemic has had profound impact on population health in the United States since March 2020. During the initial wave of the COVID-19 pandemic, countries and states issued lockdown or stay-at-home orders and hospitals began to limit nonessential procedures, surgeries, and clinic visits, to combat the rapid spread of this novel coronavirus [1-3]. Health care has been transformed in ways that could not have previously been imagined. Healthcare rapidly shifted away from in-person delivery in clinics to video encounters and telephone visits [1-5]. The American College of Radiology (ACR) has endorsed guidance from the Centers for Disease Control (CDC)

and urged imaging centers to "reschedule non-urgent outpatient imaging" [6,7]. A lot of imaging examination and procedures were canceled, deferred, or rescheduled [2,3,8-12]. For example, Vagal et al reported that approximately 30,000 studies were rescheduled during the period from March 16 to May 4, 2020 [2].

The purpose of this study is to investigate the features of MRI examinations of brain tumors in our large tertiary academic medical center during the first wave of COVID-19 pandemic. We also evaluate the association between the latest MRI findings and their prior MRI findings in the follow-up MRI examinations of patient with glioma and brain metastasis.

3. Materials and Methods

The advanced MRI techniques of MR Diffusion Tensor Imaging (DTI) and Perfusion Weighted Imaging (PWI) having been implemented as part of a routine brain tumor imaging protocol in four hospitals and outpatient imaging centers in the Department of Imaging Sciences since 2010. We retrospectively reviewed the database of these advanced MRI examinations for patients with brain tumors, which is part of an Institutional Review board –approved study. The need to obtain informed consent for this retrospective study was waived. The MRI examinations with only conventional MRI were not included in the present study.

We enrolled intra-axial tumors and large extra-axial tumors including meningioma and schwannoma in this study. March 15, 2020 was the first day that the New York state government issued stay-at home order and May 15, 2020 was the first day when the order was lifted. Therefore, we evaluated the nine-week period from March 15 to May 16, 2020 of advanced MRI examinations for patients with brain tumors. For comparison, we reviewed the advanced MRI examinations of same period in 2019.

We reviewed the electronic medical records for the age, gender, medical history, ordering clinical indication, progressive neurologic symptom, clinical and imaging impression of current imaging study, imaging findings on prior scans, and multidisciplinary discussion in brain tumor conference.

The MRI examinations were classified into "New" (brain tumor screening, new treatment planning and early post-operative MRI) and "Follow-up" according to the reason of scan. The imaging results were divided into 5 categories depending on clinical impression and MRI reports: 1) "Progression", 2) "Increased abnormality (including Increased enhancing or non-enhancing abnormality), not qualified for progression" [13,14], 3) "Decreased abnormality" (including decreased enhancing or non-enhancing abnormality), 4) "Stable or no brain mass", and 5) "Newly discovered brain mass or new treatment planning or early post-operative MRI". We calculated the "Negativity rate" as the number of MRI examinations with "Stable or no brain mass" divided by the total number of MRI examinations and the "Positivity rate" as the number of MRI examinations with the other four categories divided by the total number of MRI examinations.

Glioma and brain metastasis are most common brain tumors of routine adult brain tumor MRI examinations. The brain tumor type in our study was categorized into 1) "Glioblastoma (GBM, WHO grade IV)", 2) "High Grade Glioma (HGG, WHO grade III)", 3)" Low Grade Glioma (LGG, WHO grade I and II)" ,4) "Brain metastasis" and 5) "other brain tumors". In the clinical management of follow-up MRI examinations of glioma and brain metastasis, the imaging detection of tumor progression, or increased abnormality may warrant early intervention or modification of clinical management, while decreased abnormality and stable MRI will only warrant a further surveillance scan without immediate intervention. We assessed the "Total increased abnormalities" as the number of MRI examinations having "Progression" or "Increased abnormality, not qualified for progression". We calculate the "Percentage of Total increased abnormalities" as the number of "Total increased abnormalities" divided by the number of MRI examinations of patients with glioma and brain metastasis. For the Follow-up examinations of these patients with glioma and brain metastasis, we evaluated the imaging findings of their prior scans with four categories of "Progression", "Increased abnormality, not qualified for progression", "Decreased abnormality", and "Stable".

We compared the differences of imaging volume, age, gender, Positivity rate, and Negativity rate between 2020 and 2019 using Mann-Whitney U test and Chi-Square Test. We used Spearman's correlation to evaluate the association of latest imaging findings with prior scan result. All statistical analyses were performed with SPSS Version 19 (IBM, Armonk, New York), and p values of less than 0.05 recognized as the criteria for significance.

4. Results

For the cohort of the present study, there were no patients diagnosed with COVID-19 before and after brain tumor MRI examinations in electronic medical records till July 6, 2020.

There were 250 brain tumor advanced MRI examinations from March 15 to May 16, 2020, and 388 examinations during the same period in 2019, giving a total imaging volume decrease of 35.6%. Figure 1 shows the maximal weekly decrease in brain tumor MRI imaging were 60% in week 2 (March 22 to March 28) and 59.2% in week 3 (March 29 to April 4).

There were 81 "New" and 169 "Follow-up" examinations in 2020. During the same period in 2019 there were 131 "New" and 257 "Follow-up" examinations (Table 1).

Mean age of brain tumor advanced MRI examinations in 2020 was 58.25±15.49, and the mean age of brain tumor advanced MRI examinations in 2019 was 58.77±15.93. The imaging volume declined more in elder patients (≥70 years old) and male patients compared to younger patients and female patients, Table 1, without significant difference (p values were 0.715 and 0.145 respectively).

Table 1: Demographic information of advanced brain tumor MRI examination in 2020 and 2019.

Demographic variable	Year		Change in Imaging volume +,-
	2020	2019	
MRI examination number of all brain tumor	250	388	-35. 6%
Age <70 years old	191 (76.4%)	281(72.4%)	- 32%
Age ≥ 70 years old	59 (23.6%)	107 (27.6%)	- 44.9%
Male	126(50.4%)	214(55%)	- 41.1%
Female	124(49.6%)	175(45%)	- 29.1%
New MRI examinations	81	131	- 38.2%
Follow-up MRI examinations	169	257	- 34.2%
MRI examinations of glioma and brain metastasis	205	309	- 33.7%
GBM (WHO grade IV)	44	64	- 31.3%
HGG (WHO grade III)	19	38	- 50%
LGG	20	48	- 58.3%
Brain metastasis	122	159	- 23.3%
Other tumor	45	79	- 43%

+ indicates increase of imaging volume; - indicates decrease of imaging volume

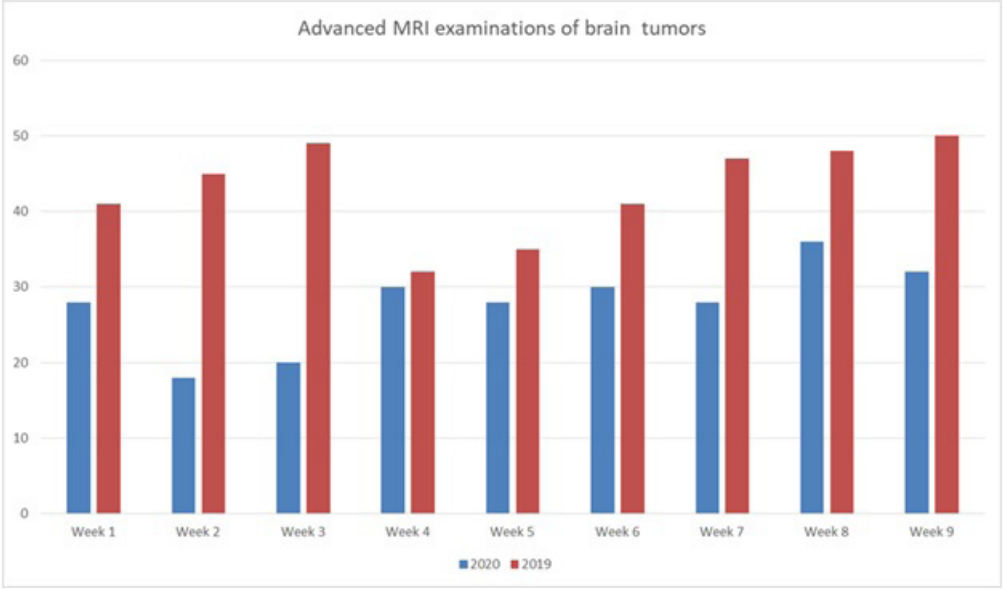

Figure 1: Weekly comparison of advanced MRI examinations of brain tumors from March 15 to May 16 in 2020 and 2019. The maximal weekly brain tumor MRI imaging volume decreases are 60% in week 2 (March 22 to March 28) and 59.2% in week 3 (March 29 to April 4).

In 2020, there were 162 "Positive" brain tumor advanced MRI examinations ("Positivity rate" was 64.8%), and 88 "Negative" MRI examinations ("Negativity rate" was 35.2%). There were 224 "Positive" brain tumor advanced MRI examinations ("Positivity rate" was 57.7%), and 164 "Negative" MRI examinations ("Negativity rate" was 42.3%) in 2019 as shown in Table 2. There was a significant difference of "Positivity rate" between 2020 and 2019, (p=0.044).

There were 205 advanced MRI examinations of patients with glioma and brain metastasis in 2020, including 44 GBM, 19 HGG, 20 LGG and 122 brain metastasis. The patients with low grade glioma had the greatest decrease of imaging volume, declining by 58.3%. The patients with brain metastasis and GBM only had 23.3% and 31.3% imaging volume decline respectively, (Table 1). Within the advanced MRI examinations of glioma and brain metastasis in 2020, there were 32 examinations were diagnosed as "Progression", and 46 examinations as "Increased abnormality, not qualified for progression".

Within 309 advanced MRI examinations of glioma and brain metastasis in 2019, there were 30 examinations diagnosed as "Progression" (without significant difference compared to 2020, p=0.546), and 51 examinations as "Increased abnormality, not qualified for progression.

The Percentage of total increased abnormalities in 2020 and 2019 were 38% and 26.2% respectively, (p=0.003, Table 2). In these advanced MRI examinations of patients with glioma and brain metastasis in 2020 and 2019, there were 159 examinations with "Total increased abnormalities". 75% of these examinations had prior MRI scan of "Total increased abnormalities". The latest imaging finding of "Total increased abnormalities" had a significant

association with the finding of "Total increased abnormalities" on the prior scan (p<0.001).

There were total 82 "stable" advanced MRI examinations of patients with glioma and brain metastasis in 2020 and 2019, of which 77 (93.9%) of their prior MRI scan were also diagnosed as "stable". The latest imaging diagnosis of "stable" had significant association with imaging diagnosis of "stable" on their prior scan (p<0.001).

Table 2: Imaging findings of advanced brain tumor MRI examinations in 2020 and 2019.

Tumor Type	Imaging finding	Year		Change in Imaging volume +,-
		2020	2019	
All brain tumors	Positive number	162	224	- 27.7%
	Positivity rate*	64.8%	57.7%	------
	Negative number	88	164	- 46.3%
	Negativity rate	35.2%	42.3%	------
Glioma and Brain metastasis	Progression	32	30	+ 6.7%
	Increased abnormality, not qualified for progression	46	51	- 9.8%
	Total increased abnormalities	78	81	- 3.7%
	Percentage of total increased abnormalities *	38%	26.2%	------
	Decreased abnormality	16	28	- 42.9%
	Stable or no brain mass	72	119	- 39.5%
	Newly discovered brain mass or new treatment planning or early post-operative MRI	39	81	- 51.9%

*indicates significant difference (p<0.05); + indicates increase of imaging volume; - indicates decrease of imaging volume;

5. Discussion

The present study showed that the total imaging volume decrease for advanced brain tumor MRI examinations was 35.6% during the period from March 15 to May 16, 2020 compared to same period in 2019. The maximal weekly drop was found in the second week (60%). There were fewer examinations in male patients and older patients (>70 years old). There were more "Positive" brain tumor examinations in 2020 than in 2019 with p=0.044. In patients with glioma and brain metastasis, there were more examinations diagnosed as "Progression" in 2020, and the Percentage of total increased abnormalities in 2020 was significantly higher (p=0.003) than 2019. The latest imaging diagnosis of "Total increased abnormalities" and "stable" had significant association with their prior imaging diagnosis of "Total increased abnormalities" and "stable" respectively, p<0.001.

COVID-19 pandemic has had a devastating impact on cancer care, including neuro-oncology treatment [15-18]. Sharpless demonstrated that modeling the effect of COVID-19 on cancer screening and treatment for breast and colorectal cancer over the next decade suggests almost 10,000 excess deaths (~1% increase) will be expected from breast and colorectal cancer deaths in the United States [18]. In neuro-oncology, neurosurgeons cancelled all nonurgent elective neurosurgeries [15-17]. Biopsies were performed in certain brain tumor patients who normally would undergo resection [16]. In patients with presumed low-grade gliomas or older patients with frailty and comorbid conditions, diagnostic surgical biopsy or resection were suggested to be safely delayed or to be abnegated [15]. Neuro-oncologists also recommended shorter courses of radiotherapy for MGMT-unmethylated gliomas and withholding temozolomide for older patients with unmethylated MGMT glioblastoma [15,19]. These treatment alterations during the first wave of COVID-19 pandemic caused suboptimal care of such patients with brain tumors.

Our present study shows that total imaging volume for advanced brain tumor MRI examinations decreased by 35.6% during the first wave of COVID-19 pandemic, which is similar with a 39% drop in imaging to evaluate stroke patients as found by Kansagra et al [20]. Our maximal weekly imaging volume drop was found in the second week (60%). Naidich et al found an overall 28% decline in the total imaging volume during 7 weeks of the COVID-19 pandemic, with the greatest decline observed for MRI (74%) and all imaging modality types (40.14%) between April 12 to18 [9]. Madhuripan et al and Vagal et al reported 46% and 53.4% decrease in imaging volume, respectively [2, 3]. In a nationwide survey, Malhotra et al revealed between a 56.4% to 63.7% decline in overall imaging volumes [11]. It should be noted that because of the highly variable severity of COVID-19 in different regions in the United States, the impact on radiology practices' volumes have varied markedly in different localities [3, 20]. The variance of reported decrease of imaging volume in different institutions is also associated with the different research period in these studies [2, 3, 9].

In the present study, we found that there were fewer examinations in older patients, which is expected as elderly patients have proven to have increased risk for COVID-19 [15-16]. It is very interesting that there was 41.1% of imaging volume decrease in male patients, which is higher than the 29.1% decrease in female patients. Griffith et al, Jin et al and Gebhard et al demonstrated that male patients have a higher mortality from COVID-19, independent of age [21-23]. The sex and gender disparities in brain tumor imaging need to be investigated in a larger and multicenter study in the future.

Our present study showed that imaging volume decline in both "New" (38.2%) and "Follow-up" (34.2%) examinations, which is associated with cancellation of elective neurosurgeries, deferment or rescheduling of non-emergent routine follow-up MRI examina-

tions for brain tumors [15-17]. The decreased imaging volume may have resulted from patients actively choosing to delay their follow-up imaging [8]. In different subtypes of brain tumors, glioma and brain metastasis accounted for 82% and 79.6% of advanced brain tumor MRI examinations in 2020 and 2019, respectively. The patients with low grade glioma had the greatest decrease of imaging volume, which is consistent with the suspension of imaging of benign and low grade tumors after the COVID-19 outbreak. The patients with brain metastasis and GBM only had 23.3% and 31.3% imaging volume decline respectively, which suggests that clinical management of these two common malignant brain tumors highly depends on imaging support beyond the telemedicine service during the COVID-19 pandemic.

In the present study, our results showed that the "Positivity rate" and "Percentage of total increased abnormalities" during the first wave of COVID-19 pandemic was significantly higher than the same period of 2019. In patients with glioma and brain metastases, our study showed increased prevalence of "Progression" 2020 (N=32, 15.6%) compared to 2019 (N=30, 9.7%). The mechanisms of these increased "Positivity rate" and "Percentage of total increased abnormalities" are complex. They may be subsequent to decreased MRI examinations of patients who have stable post-treatment brain tumors. We can't exclude the possibility of tumor progression or malignant transformation of patients with brain tumors after disruption of standard treatment, psychological burden and economic stress due to COVID-19 pandemic [11, 23].

Our findings showed substantial decline of MRI imaging volume, increased "Positivity rate" and increased "Percentage of total increased abnormalities", supporting Dr. Sharpless's statement that "there is no reason to believe the actual incidence of cancer has dropped" despite "a steep drop in cancer diagnoses in the United States since the start of the pandemic" [18]. These findings suggest potential complex and severe impact on patients with brain tumors during the first wave of COVID-19 pandemic. These characteristics demonstrate the importance and necessity to maintain "essential" MRI examinations for patients with brain tumors in the future wave of COVID-19 pandemic, as Dr. Sharpless warned, "ignoring life-threatening non–COVID-19 conditions such as cancer for too long may turn one public health crisis into many others" [18].

Because the advanced MRI techniques are part of clinical brain tumor imaging protocol in our institution, we didn't compare conventional MRI and advanced MRI in the present study. During the first wave of COVID-19 pandemic, Mossa-Basha et al shorted their MRI brain tumor protocol to 8.5 minutes of table time to reduce the risk of potential viral exposures to brain tumor patients and to increase throughput [8]. Bernhardt et al suggested that adjustments in MRI surveillance protocols should be discussed individually with the patient as it can cause significant anxiety [19]. Wen et al demonstrated that advanced MRI techniques are increasingly available to assist in the diagnosis of glioblastomas by evaluating their physiological or metabolic properties [24]. The usefulness of advanced MRI techniques in brain tumor imaging is also well established, and there are multiple diagnostic imaging challenges of brain tumors on conventional MRI compared to advanced MRI. For example, post-treatment pseudoprogression of brain glioma and brain metastasis can show similar imaging features to tumor progression on conventional MRI but can be differentiated by DTI and PWI with improved diagnostic accuracy [25]. Non-enhancing lesions that likely represent lower grade gliomas (up to 14–45% of supratentorial nonenhancing gliomas) may be malignant and behave more aggressively, which is a diagnostic dilemma on conventional MRI. By contrast, DTI has been proved to be useful in grading such nonenhancing gliomas [26, 27]. For diagnosis and treatment decision, neuro-oncologists depend on timely, accurate and comprehensive imaging evaluation. Using conventional MRI protocol alone during the COVID-19 pandemic can result in above mentioned diagnostic dilemma in patients with brain tumors, which subsequently leads to the schedule of an additional scan of advanced MRI, or a follow-up MRI of shorter interval. In contrast, advanced MRI can potentially increase the diagnostic efficiency by overcoming such diagnostic challenges as shown in a representative example in Figure 2. Therefore, we recommend advanced MRI for such brain tumor patients to support high quality neuro-oncology service. There was no patient diagnosed with COVID-19 after brain tumor MRI examinations in our study, this demonstrates that application of advanced MRI is feasible and safe for patients with brain tumors under appropriate precautions during the first wave of the pandemic.

Our present study demonstrated that the latest MRI examinations of "Total increased abnormalities" and "stable" in patients with glioma and brain metastasis had significant association with their prior imaging finding of "Total increased abnormalities" and "stable". These findings provide evidence for the development of a tiered priority system for rescheduling of imaging.

There are several limitations in this study. This was a retrospective study analyzing the database of advanced MRI in patients with brain tumors limited to a single institution. We did not include patients with brain tumors who only had conventional MRI for two reasons. First, since in our institution, most of the clinical MRI of brain tumors were scanned with the routine brain tumor imaging protocol in which advanced MRI techniques are included, we tried to minimize imaging protocol variability. Second, we compared the imaging difference between 2020 and 2019 in the present study, we tried to minimize the variance between two cohorts.

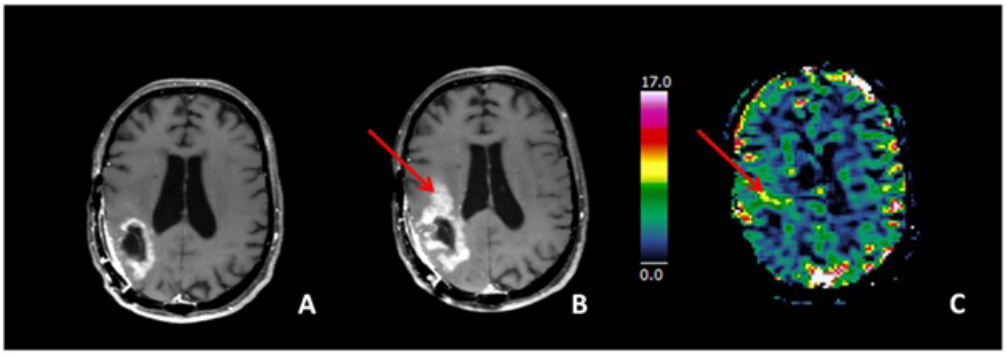

Figure 2: A GBM patient presents with enlarged heterogeneous enhancement after radiation and temozolomide, which has imaging features similar to pseudoprogression. The MR PWI shows evidence of increased perfusion in this lesion which suggests tumor progression. Figure A is prior (2 months ago) post-enhancement T1WI. Figure B is the latest post-enhancement T1WI showing enlarged heterogeneous enhancement (red arrow) anterior to surgical cavity, which has a Swiss cheese morphology (commonly see with radiation necrosis). Figure C is the relative cerebral blood volume (rCBV) map derived from MR PWI, showing high rCBV ratio in this region which proved to be tumor progression.

To best of our knowledge, this is the first study about the change in brain tumor MRI during the COVID-19 pandemic. In summary, our present study showed dramatic decrease in imaging volume of MRI in patients with brain tumors during the first wave of COVID-19 pandemic. The increased "Positivity rate", increased "Percentage of total increased abnormalities", and gender difference suggests potential complex and severe impact induced by this public health crisis on patients with brain tumors. These characteristics highlight the necessity to maintain essential pre- and post-treatment MRI examinations for patients with brain tumors in times with disruption of the clinical services including, but not limited to, the future wave of COVID-19 pandemic. The association between the latest MRI findings and their prior MRI findings provide evidence for the development of a tiered priority system for rescheduling of imaging in patients with brain tumors.

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