Usefulness of Pre-Operative Extra-Cranial Imaging in Radiologically Suspicious Glioblastoma in the West of Scotland: and a Proposal of an Imaging Diagnostic Pathway

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ABSTRACT

Objective: a CT chest, abdomen and pelvis (CT CAP) is probably unnecessary if a glioblastoma is detected on *initial* CT brain (CTB) prior to more radiologically *definitive* MRI. We audited its frequency to develop and improve our diagnostic management pathway

Methods: 12-month retrospective case series from 2018 of patients having an *initial* CTB suspicious for glioblastoma. We dichotomised patients into two groups a) Group 1: tissue proven and b) Group 2: non-tissue proven, due to increased extra-cranial co-morbidity in Group 2 which might influence a medical decision to request a CT CAP despite the radiological diagnosis of a glioblastoma being obvious on an *initial* CT. We quantified frequencies of plain and contrast CTBs, CT CAPs and extra-cranial malignancy.

Results: 131 patients had a CTB suspicious for glioblastoma. 72% had a CT CAP. 17% had extra-cranial malignancy. Group 1 (total n=84 [mean age 59 years]): 64% had a CT CAP. Plain CTB occurred in 24% and contrast CTB in 76%. Extra-cranial malignancy was 8% and 12%. Group 2 (total n=47 [mean age 73 years]): 85% had a CT CAP. Plain CTB occurred in 22% and contrast CTB in 78%. Extra-cranial malignancy was 33% and 23%. Negative CT CAPs in ~88% of CTBs in Group 1 and ~75% of CTBs in Group 2.

Conclusions: patients having an initial contrast CTB suggestive of glioblastoma, prior to definitive MRI, who are going to be managed surgically, having no history of extra-cranial malignancy, do not necessarily need a CT CAP unless MRI is non-diagnostic.

INTRODUCTION

The heterogeneous group of primary neoplastic lesions classified as World Health Organisation (WHO) grade IV glioblastoma remain the most common (~20%) of primary brain tumour in adults[1]. According to the Office for National Statistics (ONS) the incidence in England from 1995-2015 doubled from 2.4-5.0 /100,000 person-years and in Scotland ranged from 6.4-8.5/100,000 from 1993-2017[2,3,4]. Only 25% of patients survive more than a year and just 5% more than five years[1]. This is due to it being one of the most aggressive of all malignancies. It is usually first identified on an *initial* CT of the brain (CTB) before a more radiologically *definitive* magnetic resonance imaging (MRI) is done in all patients (NB: MRI is not 100% diagnostic).

Prior to MRI the differential diagnosis often includes secondary neoplastic lesions from extra-cranial malignancy. However, referral to our neurosurgical service is often always based on CT imaging prior to an MRI being done and often the radiological diagnosis of a glioblastoma is clear. Therefore, any discussion about a CT, chest, abdomen and pelvis (CT CAP) is based on CT imaging characteristics. It is at this point that a decision on CT CAP is made and our suspicion is that it is overly requested and clinically not informative.

Consequently, it has become common practice to conduct extra-cranial scans to exclude potential systemic metastatic disease even if an *initial* contrast CTB is highly suggestive of a glioblastoma and *even* once an MRI is done which provides a more *definitive* radiological diagnosis. A propensity to conduct routine extra-cranial imaging is potentially a wasteful use of resources[5,6] including time spent if a CT CAP proves to be negative in the majority (especially if this delays MDT discussion). Furthermore, a CT CAP is not recommended in the investigation of a suspected glioma as per the National Institute for Health and Care Excellence (NICE) Guidelines[7]. This is consistent to recent published evidence re-informing colleagues that a CT CAP is not useful in solitary brain lesions[8].

We decided to audit our practice to ascertain the frequency and usefulness of a CT CAP following a CTB but prior to an MRI to inform future rationalisation of our diagnostic pathway (in line with published evidence and national guidelines). These findings will also inform the development of a templated referral protocol for these patients in the West of Scotland.

METHODS AND MATERIALS

We undertook a 12-month retrospective case series from 1st January 2018 - 31st December 2018. The geographical setting was the Institute of Neurological Sciences (INS) in Glasgow, Scotland. The study was conducted according to the STROBE Statement on Cohort Studies[9] for a retrospective case series. Ethics approval was obtained from our Caldicott Guardian.

Inclusion Criteria

Our inclusion criteria included a) CTB as the *initial* imaging modality that was suggestive of a high grade intrinsic tumour prior to *definitive* MRI imaging, b) no previous history of intra-cranial malignancy and c) no previous history of cranial irradiation, d) a documented discussion at our Neuro Oncology MDT. The imaging characteristics on CTB includes, but not restricted to, a solitary intrinsic lesion, having a poorly defined border representing local invasiveness, heterogeneous contract enhancement situated more peripherally and a central hypodense aspect representing necrosis. This lesion is usually accompanied by perilesional oedema due to concomitant mass effect.

The reason to have CTB as the initial imaging modality is because it is usual practice in Scotland for a patient having neurological symptoms to have a CTB as an *initial* imaging investigation due to its ubiquitous 24-hour availability and if positive for a lesion for the on call neurosurgical registrar to then be contacted. If as neurosurgeons we consider this lesion to be highly suggestive of a high grade intrinsic tumour we then advise an MRI as the *definitive* imaging investigation to aid decision making and potential surgical planning as per NICE Guidelines[7]. However, a CT CAP is often conducted following the CTB that detected the primary intrinsic lesion prior to discussion to neurosurgery (despite this not being recommended in NICE Guidelines).

Patient Selection and Dichotomisation

This included all patients referred from West of Scotland hospitals to our quaternary neurosurgical service having an *initial* CTB suspicious for a glioblastoma prior to *definitive* MRI imaging. All patients had expert panel radiological review at our Neuro Oncology MDT. All metastatic lesions were accounted for from MDT enabling us to exclude them (as per MDT outcome based on clinical history, imaging and subsequent management, e.g. cranial or extra-cranial tissue diagnosis) to focus solely on those lesions referred to MDT considered to be glioblastoma. Patients having a CTB suggestive of a glioblastoma were then dichotomised into two groups dependent on whether they ultimately had a surgical procedure: Group 1: tissue proven glioblastoma (operated)

and Group 2: non-tissue proven glioblastoma patients (non-operated). This dichotomisation was based on our clinical experience that these groups represent distinct extra-cranial non-malignant disease patient profiles, e.g. cardiovascular, respiratory, gastrointestinal, orthopaedic, peripheral vascular and endocrine non-cancerous diseases which might influence a medical decision to request a CT CAP despite the radiological diagnosis being obvious on an *initial* CTB to exclude potential extra-cranial malignancy.

Irrespective of management both groups were discussed at a neuro oncology MDT. This has specific relevance to Group 2 as no tissue diagnosis was possible. But on detailed discussion, and expert panel radiological review, the opinion was that of a glioblastoma. If a patient in Group 1 was not discussed pre-operatively, due to significant mass effect warranting urgent surgical decompression prior to MDT discussion, on subsequent post-operative MDT discussion the radiological opinion of the *initial* CTB then MRI was always sought prior to tissue diagnosis discussion and was checked to ensure the considered opinion was that of a high grade intrinsic tumour. If diagnostic doubt existed on reviewing the initial CTB these patients were excluded from this study.

We split each group into two sub-groups if the initial CTB was a) plain or b) a contrast enhanced scan because some patients did not have a contrast enhanced scan from the outset. Subsequently, we scrutinised the frequency of CT CAPs in each group and sub-group and the rate of extra-cranial malignancy.

Data Collection

We identified patients from two sources a) the neurosurgical on call electronic referral database and b) the West of Scotland neuro-oncology multi-disciplinary Team (MDT) meeting to enable complete data capture. We searched case notes in NHS Greater Glasgow & Clyde and Scottish National Picture Archiving and Communication System (PACS) to ensure identified patients met our inclusion criteria. The data was collected by two experienced senior house officers in neurosurgery and double checked by a senior neurosurgical registrar from 1st December 2019 – 31st May 2020 independent of each other.

Bias

Potential sources include data extraction and incomplete medical documentation. We minimised this by having independent data collection by RMcP and EB. This was independently double checked by SL. Data was extracted

from two electronic NHS Scotland patient platforms called TraKCare 2018 and Clinical Portal. These contains every single nursing, medical, radiological and anaesthetic entry both written and electronic.

Statistical Analysis

We quantified the usefulness of CT CAPs in the pre-operative work up of patients radiologically diagnosed with a glioblastoma according to our pre-determined inclusion criteria. Within our two sub-groups we compared the rates of CT CAPs in patients with plain CTB to those with contrast enhanced CTB. We carried out the analysis in patients with and without a previous history of extra-cranial malignancy. We carried out a two-sample t-test for parametric data and a Chi-squared test for proportions based non-parametric data using IBM's Statistical Package for the Social Sciences (SPSS)[10].

RESULTS

A total of 131 patients were referred to our neurosurgical service with an *initial* CTB suspicious for a glioblastoma. The mean age was 64 years (range: 20-88 years). The 30-Day mortality was 8% (n=10). A total of 72% (n=94) had a CT CAP. Of these 17% (n=16) were positive for potential extra-cranial malignancy. Overall 11% (n=14) of patients had a previous history of extra-cranial malignancy and 100% had a CT CAP. Of these patients 14% (n=2) had a positive CT CAP (see Figure 1 and Figure 2). This means 13% (n=2) of positive CT CAP patients had previous extra-cranial malignancy. A CT CAP only influenced management in 1% (n=1) of patients. We then analysed these results according to our group dichotomisation paying particular attention to CT CAP requests between Group 1 (64%) and Group 2 (85%).

A comparative statistical analysis of age, frequency of plain and contrast CTBs, anatomical distribution of glioblastomas and frequency of CT CAPs and concomitant frequency of extra-cranial malignancy between Group 1 and Group 2 are summarised in Table 1. This demonstrates a statistically significant difference between both groups regarding mean age ($p < 0.05$) and frequency of CT CAPs ($p < 0.05$, X^2 6.48, 95% CI 5.09-34.05%). The anatomical distribution and radiological features on CTB were similar between both groups and are demonstrated in Figure 3 and Figure 4. These were non-statistically significant as demonstrated in Table 1. The group specific results are presented in turn.

Group 1: Tissue Proven Glioblastomas (Operated)

84 patients underwent neurosurgical intervention. The male to female ratio was 1:1.1 and mean age 59 years and median of 61 years (range: 20-78 years). The 30-day mortality was 5% (n=4). A total of 64% (n=54) had a CT CAP. Of these 9% (n=6) were positive for potential extra-cranial malignancy. Overall 10% (n=8) of patients had a previous history of extra-cranial malignancy and 100% had a CT CAP. Of these 13% (n=1) had a positive CT CAP. This means 17% (n=1) of positive CT CAP patient had previous extra-cranial malignancy (see Figure 1 and Figure 2). If we analyse these according to CT CAP requested from plain and contrast CTBs we get this following breakdown.

An initial plain CTB occurred in 26% (n=22) and a contrast CTB in 74% (n=62). The proportion of tumours on a contrast CTB demonstrating contrast enhancement was 94%. Of these 59% (n=13) of plain CTBs and 66% (n=41) of contrast CTBs had a CT CAP. Of these 8% (n=1) and 12% (n=5) were positive for potential extra-cranial

malignancy respectively. These required follow up but did not delay neurosurgical management. A further 15% (n=2) of plain CTBs and 10% (n=4) of contrast CTBs had CT CAP imaging demonstrating radiological findings which were investigated and found to be benign (see Figure 5). This means 92% of plain CTBs and 88% of contrast CTBs who had a CT CAP was negative for malignancy.

Of the eight patients who had a previous history of extra-cranial malignancy two had a plain CTB of which n=1 (50%) had a positive CT CAP and six had a contrast CTB of which n=0 (0%) had a positive CT CAP. Overall, 13% of these patients had a positive CT CAP. 64% (n=54) of these surgically managed patients had a CT CAP following their *initial* CTB and prior to *definitive* MRI imaging. Incidentally, 64% of CT CAPs were requested by a neurosurgeon.

Group 2: Conservatively Managed Glioblastomas (Non-Operated)

47 patients did not undergo neurosurgical intervention due to co-morbidities, age-related frailty and poor performance status. The male to female ratio was 1:1.35 and mean age 73 years and median of 74 years (range: 33-88 years). The 30-day mortality was 13% (n=6). A total of 85% (n=40) had a CT CAP. Of these 25% (n=10) were positive for potential extra-cranial malignancy. Overall 13% (n=6) of patients had a previous history of extra-cranial malignancy and 100% had a CT CAP. Of these 33% (n=2) had a positive CT CAP. This means 20% (n=2) of positive CT CAP patient had previous extra-cranial malignancy (see Figure 1 and Figure 2). If we analyse these according to CT CAP requested from plain and contrast CTBs we get this following breakdown.

An initial plain CTB occurred in 28% (n=13) and a contrast CTB in 72% (n=34). The proportion of tumours on a contrast CTB demonstrating contrast enhancement was 85%. Of these 69% (n=9) of plain CTBs and 91% (n=31) of contrast CTBs had a CT CAP. Of these 33% (n=3) and 23% (n=7) were positive for potential extra-cranial malignancy (see Figure 6). In these ten patients, metastatic disease which was not amenable to extra-cranial surgical intervention in five patients, and poor performance status in the others, ruled out neurosurgical management. A further 11% (n=1) of plain CTBs and 16% (n=5) of contrast CTBs had CT CAP imaging demonstrating radiological findings which were investigated and found to be benign (see Figure 4). This means 67% of plain CTBs and 77% of contrast CTBs who had a CT CAP was negative for malignancy.

Of the six patients who had a previous history of extra-cranial malignancy two had a plain CTB of which n=1 (50%) had a positive CT CAP and four had a contrast CTB of which n=1 (25%) had a positive CT CAP. Overall, 33% of these patients had a positive CT CAP. 85% (n=40) of these conservatively managed patients had a CT CAP following their *initial* CTB and prior to *definitive* MRI imaging. Incidentally, 50% of CT CAPs were requested by a neurosurgeon.

Unexpected Results

Nine (19%) patients initially managed conservatively based on clinical assessment and functional status subsequently went on to have a cranial procedure and had an alternative diagnosis confirmed: n=5 had a biopsy (80% negative CT CAP) and n=4 had a craniotomy (75% negative CT CAP). Of these n=3 were WHO II/III glioma, 2 metastatic, 2 haemorrhagic, 1 abscess and 1 Epstein Barr (EBV) virus.

DISCUSSION

Overall, a CT CAP was performed in 72% of patients in our case series. Of these 17% had a suggestion of radiological extra-cranial malignancy on CT CAP. If assessed according to our dichotomisation this split becomes 9% in Group 1 and 25% in Group 2. In Group 1 a CT CAP if ordered was negative for malignancy in 92% of plain CTBs and 88% of contrast CTBs. In Group 2 a CT CAP was negative for malignancy in 67% of plain CTBs and 77% of contrast CTBs. This demonstrates a high rate of negative scans in Group 1 and in Group 2 if compared to positive findings associated in each group and type of CTB. The reason for dichotomising CTBs into plain and contrast scans was to demonstrate that even a plain CTB translated into a high rate of negative CT CAP. Naturally, contrast yields a firmer diagnosis of glioblastoma and is therefore more likely to be associated to negative systemic imaging than plain CTBs. This is seen in Group 2.

A quick and accurate diagnosis of a glioblastoma is crucial to enable both timely and appropriate management. This could be surgical management, e.g. biopsy, sub-total resection or gross total resection, followed by chemo-radiotherapy or conservative management, e.g. palliation. An *initial* CTB offers a high degree of reliability of a radiologically suspicious high grade glioma prior to *definitive* MRI imaging[9]. Multiple radiological characteristics help to increase certainty of a diagnosis. These include heterogeneous contrast enhancement, vasogenic oedema and concomitant mass effect. In conjunction with the clinical history a robust radiological diagnosis of a glioblastoma especially on *initial* contrast CT can be made[11,12].

In Glasgow a new diagnosis of a neoplastic brain disease results in a patient being referred from their local hospital to the on call neurosurgical registrar phone. The neurosurgical registrar then submits a patient proforma for discussion at our weekly neuro oncology MDT.

In our results 94% of contrast CTBs in tissue proven glioblastomas (Group 1) and 85% of non-tissue proven glioblastomas (Group 2) demonstrated an enhancing lesion radiologically consistent with a glioblastoma on expert panel review at MDT. This can be seen prior to their definitive MRI imaging. Therefore, almost all contrast CTBs in Group 1 and the overwhelming majority in Group 2, on *initial* neurosurgical review, can be interpreted radiologically to be a glioblastoma. Interrogation of the on call neurosurgical registrar notes and neuro oncology MDT meeting minutes reveals a concordant opinion of a glioblastoma diagnosis in almost all those patients discussed that incidentally did not have definitive MRI imaging (NB: concordance of a glioblastoma diagnosis

existed for all patients at our neuro oncology MDT). Where the initial CTB was reported by a general radiologist prior to the neuro oncology MDT a wider differential diagnosis sometimes prompted a CT CAP. However, 64% of Group 1 and 50% of Group 2 CT CAPs were requested based on advice from the on call neurosurgical team, despite an initial CTB being highly suspicious for primary high grade disease.

There may be a cultural perception that a CT CAP should be performed prior to MDT discussion, but where this imaging was not available discussion took place regardless and most decisions are made without it. The presence of a CT CAP did not affect decision making at all in Group 1 (due to a better performance status, minimal co-morbidities and surgical intervention being the best option for their intrinsic lesion) and only impacted upon the clinical management of one patient in Group 2. This patient subsequently had a craniotomy and resection of a histopathologically proven metastatic tumour in a delayed fashion.

Delays in decision making and treatment in this series attributable to a perceived need for systemic imaging were observed in 10% of cases in Group 1. One patient waited six days for a CT CAP following a contrast CTB. This delayed MDT discussion for two weeks from point of original CTB (NB: of these 10% of patients in Group 1, the mean extra delay was one week and the maximum delay was four weeks for extra-cranial systemic medical imaging). Treatment delays can result in adverse outcomes for patient's[13]. Delayed surgical intervention can allow unfortunate tumour expansion, a sub-total resection, worsened pre- and post-operative performance status and subsequent delays to adjuvant oncology.

Signs of extra-cranial malignancy were demonstrated in just 8% (n=1) and 12% (n=5) of plain and contrast CTBs in Group 1. These findings did not change management nor warrant further investigation (or treatment). In one patient who had a lung malignancy investigated by bronchoscopy (an adenocarcinoma was eventually diagnosed) this did not take precedence over their glioblastoma and no delay occurred regarding neurosurgical management. Our study highlights that two of the most common reasons to conduct CT CAPs is to assess for presence of a) widespread systemic malignancy and b) malignancies which have a high propensity for intra-cerebral dissemination, e.g. small cell lung cancer, does not exist in Group 1.

The finding of a statistically significant higher mean age ($p < 0.05$) and increased frequency of a CT CAP in Group 2 ($p < 0.05$, X^2 6.48, 95% CI 5.09-34.05%) is not surprising. With increasing age come decreased performance

status, increased frailty and increased co-morbidity making surgical intervention a less attractive and higher risk endeavour. Age also brings a higher likelihood of occult extra-cranial disease. Therefore, the lower mean age of 59 years in Group 1 and concomitant decreased clinical suspicion of systemic malignancy explains the lower frequency of 64% getting a CT CAP. Consequently, the higher mean age of 73 years in Group 2 and increased clinical suspicion of systemic malignancy that comes in advanced age explains the higher frequency of 85% getting a CT CAP.

Signs of extra-cranial malignancy were demonstrated in 33% (n=5) and 23% (n=7) of plain and contrast CTBs in Group 2. This is a higher proportion than expected as just 13% had a previous history of extra-cranial malignancy. Therefore, a CT CAP is perhaps not an unreasonable request in Group 2 as opposed to Group 1[14]. In this group, the frequency of a negative CT CAP was 67% for those having a plain CTB and 77% for those having a contrast CTBs and is not as high as in Group 1. This study is therefore unable to support managing this group without systemic imaging, particularly where the only brain imaging is a plain CT scan. This decision will depend on the overall clinical situation for individual patients.

This case series suffers from the known limitations of retrospective studies. We intentionally focused on CTBs and not MRIs due to CTB being the initial test and to analyse if a glioblastoma is that obvious on initial imaging. We found nine patients who were conservatively managed who subsequently had operative intervention which confirmed an alternative histopathological diagnosis despite the initial CTB being highly suggestive of a glioblastoma.

A concern, particularly in Group 1, is that a craniotomy, gross total resection and concomitant neurological risk, is a serious undertaking for a patient to go through if occult extensive extra-cranial malignancy is subsequently diagnosed post-operatively. Although this is extremely rare as our data highlights (NB: non-existent in our group) if this occurs in one patient the personal cost to the patient and financial ramifications of changing their management potentially outweighs the reflexive decision to conduct a pre-operative CT CAP. A prospective study might better define the proportion of these cases and whether obtaining systemic imaging prior to surgery influences decision-making for this group or whether it can be performed post cranial surgery with no detriment to clinical care.

In this series, the frequency of known extra-cranial malignancy prior to their glioblastoma presentation in Group 1 was 10% and of this subset of patients just 13% had evidence of ongoing malignant disease on CT CAP. Furthermore, despite overlapping age ranges between both groups, 20-78 years in Group 1 and 33-88 years in Group 2, both the mean age in Group 1 of 59 years and calculated median of 61 years was lower than the mean of 73 years and median of 74 years in Group 2. However, from the present series we cannot extrapolate this difference in mean and median ages to suggest an age criterion for including a CT CAP in pre-operative investigations, as this is a question for another study.

Another consideration is a cost and resource implication of unnecessary CT CAPs. A full economic evaluation of the impact of reducing the number of CT CAPs undertaken would need to consider not only the cost savings to radiology departments from CT CAPs themselves, but also the reduction in costs of care incurred while patients remain in hospital awaiting results, e.g. nursing, medical and transportation costs. Consequently, the potential saving of £103 per CT CAP[15] does not represent the fuller cost around the entire patient pathway. The impact on health outcomes would also need to be considered including the impact of patient anxiety regarding diagnosis and management, as it has been proven that extensive investigation can cause unnecessary stress for patients[16]. Such an economic evaluation is beyond the scope of this paper.

One reason for such indiscriminate use might be due to an age-old culture of on call neurosurgical advice for referring teams to request a CT CAP simultaneously to that of an MRI brain prior to definitive surgical decision making occurring. So, over time referring teams request a CT CAP once a CTB is done prior to neurosurgical discussion to enable a smoother conversation.

Therefore, based on the current study a recommendation can be made that patients meeting the following criteria do not require CT CAP prior to surgical intervention (especially as ~75% of patients had an *initial* contrast CTB): 1) if an *initial* contrast CTB is highly suggestive of high grade glioma, 2) planned surgical management is expected to yield a tissue diagnosis from the brain lesion, 3) no history of previous extra-cranial malignancy exists (see Figure 7). If we restrict this protocol to Group 1 (because as previously mentioned this study is unable to support managing Group 2 without systemic imaging) this means only one patient having a CT CAP out of forty four. This would prevent 43 CT CAPs from occurring having a potential saving of £4,429 (NB: as mentioned above a CT

CAP costs £103 but this does not represent the fuller cost around the patient pathway, e.g. portering, nursing, radiography, radiology costs and impact on patient anxiety around imaging)

A further refinement of this suggested imaging pathway factors in plain CTBs. If an *initial* imaging modality is a plain CTB a patient should probably continue to have a *definitive* MRI instead of a contrast CTB. This avoids a potentially unnecessary dose of contrast and radiation. The caveat is that if a patient who has deteriorating neurology is referred and needs an urgent surgical decision regarding mass effect then a contrast CTB might be warranted to characterise the lesion to optimise surgical decision making (see Figure 8). This is because a *definitive* MRI in these patients is not straightforward to get especially out of hours. Otherwise, a lesion on plain CTB should prompt a *definitive* MRI during normal working hours unless a patient cannot tolerate it. Therefore, a contrast CTB can be done.

We postulate that a CT CAP then should only be done according to our earlier postulation a) an *initial* plain and contrast CTB is highly suggestive of a glioblastoma and a delay exists in conducting a *definitive* MRI, b) an MRI is non-diagnostic (this would introduce a treatment delay but the number of CT CAPs requested in this context would be offset by the number not needing a CT CAP according to our protocol), c) a patient has a previous history of extra-cranial malignancy and d) a patient is not suitable for surgical management due to advanced age and frailty. This could reduce the number of patients' undergoing unnecessary scans, understandable anxiety, potential delays to treatment and preserve access to CT scanning for other patient groups.

CONCLUSION

Our case series suggests that patients who especially have a contrast CTB as their initial imaging modality which is highly suggestive of a glioblastoma, who are going to be managed surgically, having no previous history of extra-cranial malignancy, do not need a CT CAP unless their diagnostic pathway recommends it as the positive yield is so low.

DECLARATION OF INTERESTS

None

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AUTHOR CONTRIBUTIONS

SL (Conceptualization; Methodology; Software; Formal Analysis; Investigation; Resources; Writing – Original Draft; Visualization; Supervision) prepared the Introduction. SL prepared the abstract, methods, results and discussion (and formulated the Tables and Figures). RMcP and EB (Writing – Review & Editing; Visualization) scrutinized the whole manuscript and double checked it for accuracy and fluency. RMcP and EB (Investigation) extracted the data for 2018 which was independently checked by SL. JB (Writing – Review & Editing) provided a structured critique regarding language and overall analysis of the thrust of this manuscript. JB provided expert commentary and conceptualization

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FIGURES

Fig. 1: This is a flow diagram of the number of CT CAPs requested from the total, Group 1 and Group 2 patients.

Fig. 2: This demonstrates a graphical representation of Figure 1 enabling the lower request rate of CT CAPs in Group 1 to be compared to the relatively much higher request rate of CT CAPs in Group 2.

Fig. 3: This demonstrates the relative anatomical frequency of glioblastoma s if compared between the two groups.

Fig. 4: This demonstrates the relative frequency of radiological features of glioblastoma on CT between the two groups.

Fig. 5: This is a flow diagram of CT CAPs in Group 1 (NB: pCTB = plain CTB and cCTB = contrast CTB)

Fig. 6: This is a flow diagram of CT CAPs in Group 2 (NB: pCTB = plain CTB and cCTB = contrast CTB)

Fig. 7: A flow diagram of a suggested imaging pathway in radiologically suspected glioblastoma on a contrast CTB

Fig. 8: A flow diagram of a suggested imaging pathway to minimise use of contrast CTBs