1 The Neuroscience of Brain Tumors

Brain tumors are a mass of cells that grow abnormally in the brain tissue, and serve no (good) purpose. Benign tumors grow slowly, and usually do not invade the other parts of the brain, unlike malignant tumors, which spread fast, and overgrow cancerous cells and harm normally-helpful cells (Harvard Health Publishing, 2019; Ambardekar, 2019). While these tumors make up for only 1.8% of the overall incidence rate of cancers, they prove to be more mortal than the rest of the cancers (Ferlay et. al, n.d.).

1.1 The Neurobiology

Depending on where the cell growth starts, we observe different tumors, such as, glioma (overgrowth of glial cells, which surround neurons), meningioma (overgrowth of meninges, which cover and protect the brain under the skull), pituitary (overgrowth of the cells in pituitary gland, known as the main hormone-produce organ of the human body), etc (John Hopkins Medicine, n.d.). Since cancerous cells spread quickly, brain can be prone to secondary tumors as well, coming from the lung, breast or skin cancers (Nature, n.d.). These tumors are called metastases, since the cancerous cells are not brain cells (but inherited from other organ, i.e skin cells), and the spread happens through blood circulation or lymphatic system (Cancer Research UK, n.d.). Tumors are defective because the spread of cancerous cells disrupts the growth of normal cells by **(1)** not allowing the old cells to die, and **(2)** creating excessive unnecessary cells. Both disruptions disable the brains to function normally, since normally old cells divide to create new functioning cells, but cancerous cells divide without inheriting the same functionality (Cancer Research UK, n.d.). [1]

1.2 The causes and interventions

Malignant tumors are only observed after overgrowth, which is often too late to intervene. As to what causes them, there is no conclusive evidence. Several hypothesis suggest that brain tumors develop from genetic mutations carried with DNA, while the rest suggest that environmental toxins, diet, stress, infection and local trauma could be causal factors (Ambardekar, 2019). Most of the doctors agree that different tumors are not always caused by one factor, rather the same tumor could be caused by different factors in two different people, or sometimes a combination of factors. As such, both the type of the intervention and the timing of the intervention remain difficult to decide. Nevertheless, it is established that the effects of these causes are overgrowth of cells, thus methods that reduce the cell growth (i.e. radiation and chemotherapy) have proven effective (AANS, n.d.). Depending on the location of the brain tumor and the grade of the tumor, surgery could also pose a good candidate solution. However, surgery is highly invasive, therefore, it could do more damage by deteriorating other parts of the brain while trying to remove the tumor, especially when the tumors are located in the inner brain. Unfortunately, well-developed tumors are often incurable. Tumors have several effects of physical, cognitive and behavioral nature. Some of the symptoms are (AANS, n.d.):

- Physical: Severe headaches, seizures, paralysis, nausea, vomiting, facial numbness,
- Cognitive: Difficulties with thinking, speech formation and recognition, vision/hearing changes,
- Behavioral: Confusion, disorientation, personality changes, depression.

Especially when tumors are terminal, it can be difficult information to process for the patient, hence causing major changes in one's social life. This impacts not only the patient, but their families as well; emotionally and financially. Brain tumors have the highest per-patient initial cost compared to any other tumors, rounding at 150,000 USD (Halkin, 2018). As follows, the latter stages of development, the higher the economical costs.[2]

1.3 Brain Tumor Detection

Brain tumors are difficult to detect before they progress. Any misdiagnosis could be detrimental; not diagnosing a real tumor means that the tumor will progress, and misdiagnosing cell growth for a tumor, could meant that patient will take treatment that would kill their healthy cells. The gold standard for detection remains histopathology (biopsy), where a live brain tissue undergoes a molecular analysis to determine the presence of a tumor (Gao Jiang, 2013).

[1] #NeuralSubstrate: I explain where the tumor appears, and how it spreads, while noting why the overgrowth of cells and their spread is defective to the brain.

[2] #AetiologyImpactandIntervention: I explained the potential causes of the tumor and how they're linked with the intervention decisions (whether there should be an intervention, the timing and the type), and then I explain the effects of having a brain tumor physically, cognitively, behaviorally, socially and economically.

Progression in detection involve neuroimaging techniques, which are less invasive, and reduce the chance of extracting live tissue merely based on patient's history.

1.4 MRI

Magnetic Resonance Imaging shows to have one of the best performance in tumor detection. Using magnetic field and radiowaves, MRI is able to create images of brain areas that cannot be seen with CT-scans or X-rays. What makes MRIs a good detection tool is:

- Non-invasiveness
- Good spatial resolution: It is crucial for tumor detection to have a clear picture of the soft tissue
- Not using radiation: Radiation can be detrimental if used incorrectly, especially for potential tumor patients

However its sensitivity (precision) has been reported to comparatively low to more advanced techniques Lately, advanced contrast agents have been introduced which improve its sensitivity slightly (Gao Jiang, 2013). When combined with optical imaging (that has a high sensitivity and specificity), MRI could help locate "hidden"tumors with higher accuracy (Gao Jiang, 2013). [3]

1.5 Machine Learning

Another pitfall of this method is the human error - doctors read the scans. While there are well-established guidelines on reading neuroimages (i.e. obtaining a second opinion), this human error could be mitigated. With the machine learning classification, we could use previously correctly-labelled MRI neuroimages, and train the machine to output the diagnosis in either the form of binary classification:

No Tumor — Tumor

or multi-class classification:

No Tumor—Tumor: Tumor1-Tumor2-Tumor3...

These are probabilistic models, which means that they are **not** always accurate, but we could know quite precisely the margin of error, which is difficult to measure in human judgement. Machine Learning models could be used with doctor's judgement in a complementary manner. A complete example of how these models work is in this code. [4]

2 Neuroscience-based recommendations

There is a considerably big amount of research in brain tumors as a whole - but not as much about their detection. While it is important to know how to treat a tumor, and especially understand where it is coming from, the tumor, or the lack thereof, must first be confirmed with high accuracy. Considering the high mortality rate, the impact of brain tumor in everyday life and the problems with detection of tumors, I propose that more research should be funded in two directions, when it comes to brain tumor detection:

1. Improving neuroimaging techniques:
   (a) For instance, finding contrast agents that improve the sensitivity and specificity of the MRI scans.
2. Integrating computerized diagnosis:
   (a) This could improve with reducing the human error and having higher certainty in diagnosis.

The first direction will help us advance already-used techniques, which is helpful because the doctors are already used to these techniques and would not need an excessive amount of extra training given there is an advancement.The second direction, proposes to merge two fields which have been seen as separate for a long time. Using Machine Learning models for detection could reduce the risks of misdiagnosing - or at least quantify the risk, by producing objective metrics of judgement, compared to human judgement which cannot be assessed in quantity. [5]

Word Count: 1084 words + code (800 words).

[3] #ConvergingApproaches: I note down the advantages of MRI in the context of brain tumor detection, alongside the points for improvement. I propose improving the sensitivity with a complementary approach (optical imagining) on top of improving contrast agents.
[4] This is my CS156 Part of the Assignment. You can find a reader-friendly version under the Data Visualization file.
[5] #NeuroethicsNeuroscienceAndSociety: I explain two potential gaps in the tumor detection field, and propose how to mitigate them by funding more research on these topics. I provide a rationale to how these suggestions might improve the current tumor detection field.

3 References

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