



## **Diagnostic Conundrum: Recurrence or Postoperative Inflammation in A Case of Oral Carcinoma**

Dr. Jitendra Kumar Sharma<sup>1</sup>, Dr. Poonam Joshi <sup>2\*</sup>, Dr Teertha Shetty <sup>3</sup>, Dr. Sudhir Nair <sup>4</sup>,  
Sayak Choudhury<sup>5</sup>, Dr Pankaj Chaturvedi <sup>6</sup>

1. Senior Resident, Department of Head and Neck Surgery, Tata memorial hospital, HBNI, Mumbai
2. Associate Professor, Department of Head and Neck Surgery, Tata memorial hospital, HBNI, Mumbai
3. Follow, Department of Head and Neck Surgery, Tata memorial centre, Mumbai
4. Professor, Department of Head and Neck Surgery Tata memorial hospital, HBNI, Mumbai
5. Assistant Professor, Department of Nuclear medicine, Tata memorial hospital, HBNI, Mumbai
6. Professor, Department of Head and Neck Surgery Tata memorial hospital, HBNI, Mumbai

**Corresponding Author: Dr. Poonam Joshi**, Associate Professor, Department of Head and Neck Surgery, Tata memorial hospital, HBNI, Mumbai

**Copy Right:** © 2022 Dr. Poonam Joshi, This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Received Date: July 28, 2022**

**Published Date: August 05, 2022**

## Introduction

In the early postoperative period, the reparative mechanism involves inflammation followed by formation of granulation tissue and subsequently, fibrotic changes. Occasionally, these changes can mimic as recurrent tumour in the postoperative bed. Even with the availability of advanced imaging modalities these changes sometimes can lead to a diagnostic dilemma. Although, a positive biopsy is confirmatory, a negative biopsy cannot exclude the disease. Here, we present a case of oral carcinoma treated with surgery who presented with clinicoradiological inflammatory changes masquerading as recurrence. The high focal FDG uptake on PET-CT added to the dilemma.

Case presentation: A 39-year-old male patient, reformed chewer, without any comorbidities presented to the head and neck outpatient department with the complaint of ulcer in the left side of the oral cavity. He had undergone an excisional biopsy one month back and was reported as squamous cell carcinoma (SCC). On examination, a 1x1 cm ill-defined lesion was seen involving left buccal mucosa. RMT, upper and lower GBS were not involved.

CT Head and Neck showed 1.8x0.5x1.1cm, heterogeneously enhancing lesion seen involving left buccal mucosa. ( Figure 1) All muscles of mastication were free and there was no bone erosion. There were no suspicious nodes. An ill-defined nodule of 0.8x0.9x0.9 cm size with a peripheral rim of calcification in the right lobe of the thyroid was detected incidentally. USG guided FNAC of thyroid nodule was suggestive of follicular neoplasm of undetermined significance (Bethesda 3).

The patient underwent wide local excision of buccal mucosa with left I-III neck dissection and skin graft. In view of papillary carcinoma nodes detected on frozen, total thyroidectomy with right central compartment clearance was done on 5\4\2021. The post-operative period was uneventful. On final histopathology, no residual tumour was identified in the buccal mucosa and was kept under observation. The patient was planned for RAI therapy in view of positive central compartment nodes. The patient was kept hypothyroid for RAI therapy. While awaiting for RAI, the patient presented to our outpatient department with a suspected lesion in the left buccal mucosa and swelling over the face after 8 weeks of surgery.

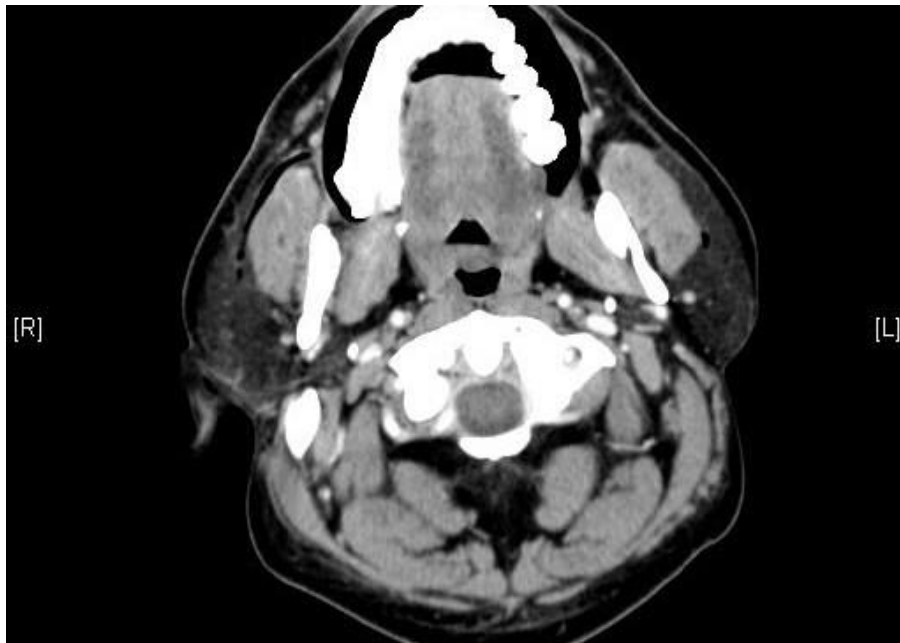
On examination, suspicious ulceration was seen amidst granulation tissue-like lesion with underlying induration. The epicentre was left buccal mucosa extending posteriorly till left RMT and anteriorly reaching till canine region, involving both upper and lower GBS. Oedema of the overlying skin reached till zygoma (Figure 2). No palpable neck nodes were found.

PET CT was done which was suggestive of focal FDG avid lesion of size 1.4x1.6 cm (SUV max 14.36) involving upper GBS with subtle cortical erosion along the outer surface of the in background of intense post-operative oedematous changes in left buccal space (Figure 3) . Knife biopsy was taken from the suspicious ulcerative area and was reported as granulation tissue. MRI was also done which showed an ill-defined 17x11x10mm, T1 isointense, STIR hyperintense enhancing lesion with epicentre in the left buccal mucosa, involving the upper and lower GBS, buccal space, and reaching up to the RMT (Figure 4) . There was early enhancement on dynamic post-contrast imaging and was reported as suspicious for malignancy.

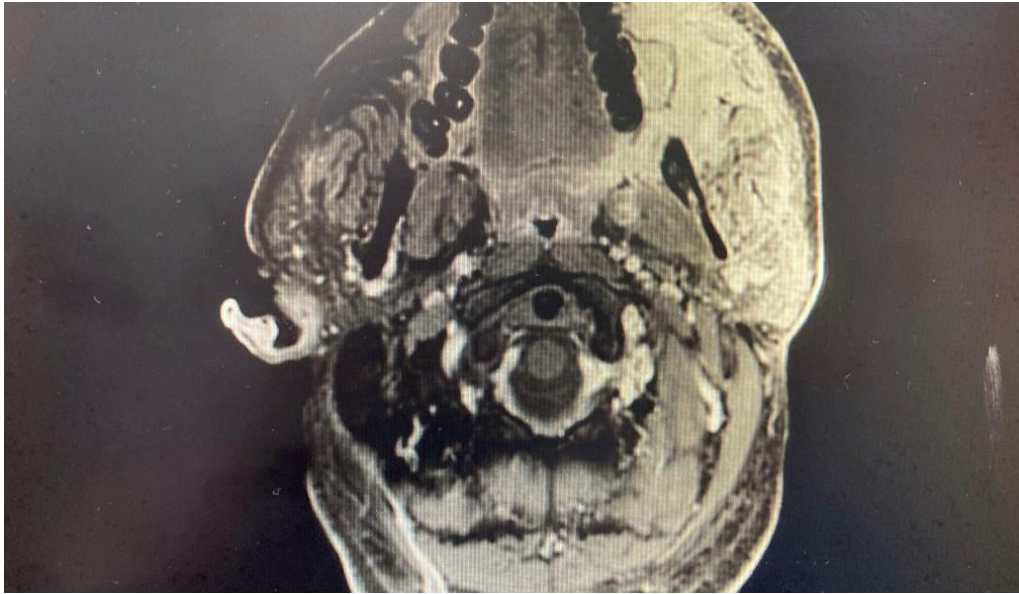
In view of suspicious clinical and radiological findings (PET CT and MRI), CT guided biopsy was done from a focal enhanced area (SUV max 11.43). Biopsy from the lesion was negative.

Nonetheless, in view of strong clinical suspicion and positive radiological findings, the decision for surgery vs observation was discussed with the patient. As the tissue diagnosis was negative twice and an extensive surgical resection was needed, a decision was taken to keep the patient under observation. The patient was started on Tab Clindamycin 600 mg TDS, Tab Trypsin Chymotrypsin TDS, Tab Thyroxine 150mcg OD for 15 days. After 15 days, there was a decrease in oedema over the face. Hence, antibiotics were discontinued, and the patient was kept under observation.

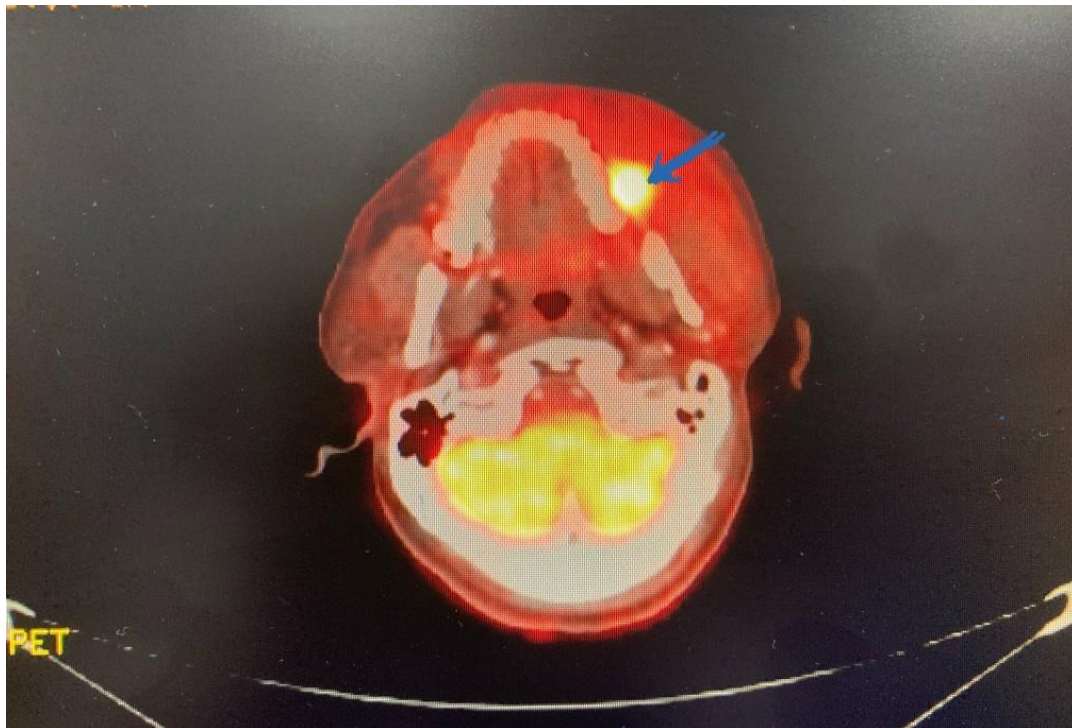
PET CT scan was repeated after 4 months of surgery, showing a significant decrease in FDG uptake (SUV max 5.5), and clinically significant decrease in oedema and size of lesion at the operated site (Figure 5). Thus, in view of negative biopsy and low uptake on PET, it was considered as postoperative.



**Figure 01: Preoperative CT image**



**Figure 02: MRI post-surgery 8 weeks**



**Figure03: PET in early post operative period at 8 weeks showing high focal FDG uptake(SUV max 11.43) marked with arrow**

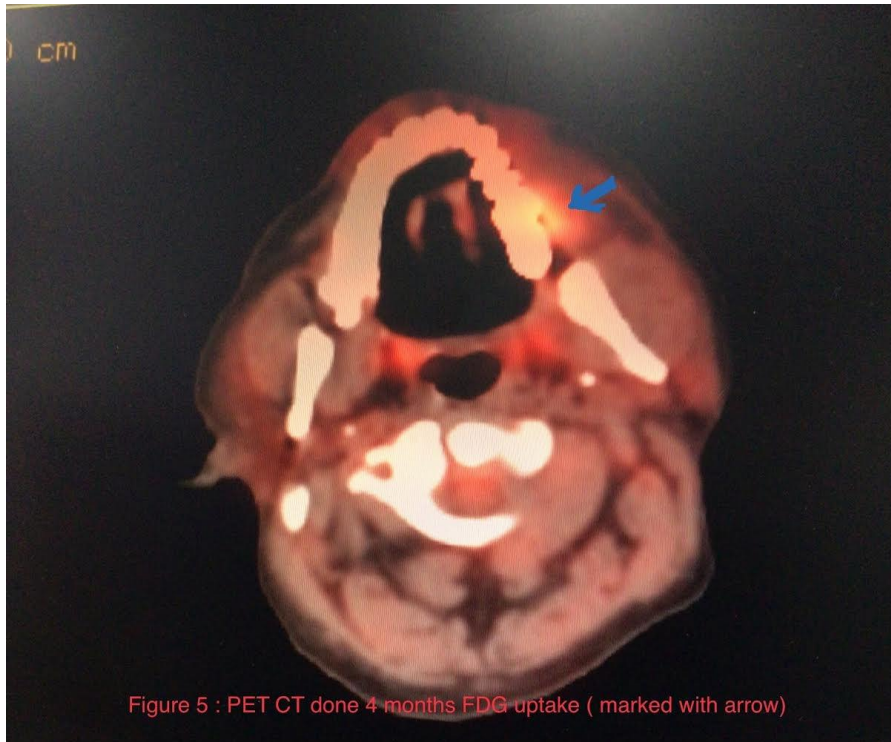


Figure 5 : PET CT done 4 months FDG uptake ( marked with arrow)



**Suspicious lesion on left buccal mucosa**



**Oedema over the face**



**Post operative 1 year follow up showing hypertrophied scar on the left buccal mucosa**

## Discussion

Imaging-based detection of disease recurrence in head and neck squamous cell carcinoma can be performed using various modalities like CT, MRI, PET CT, and ultrasound. While, MRI has good sensitivity (70-100%), the specificity is poor ranging from 41% to 54%. CT has a wider range with moderate sensitivity (50% to 86%) and specificity (33% to 100%).[3] USG is mainly used in surveillance for nodal recurrence in the neck. USG has several advantages over CT and MRI as it is cost effective, there is no radiation exposure and guided FNAB can be done in the same sitting.

Reported sensitivity, specificity, positive predictive value and negative predictive value of USG in detecting nodal recurrence when combined with FNA is 80%,100%,100%, 92.3% respectively. The diagnostic accuracy of ultrasonography guided FNA at detecting residual persistent cancer is 88%. [8] However, it is not an appropriate imaging tool for oral cavity recurrences.

MRI has incremental value over CT scan in assessment of tumor recurrence and differentiation from post-surgery changes.[7] T2 signal intensity within the treated field can be used to distinguish between scar and recurrent neoplasm, although both may demonstrate post-contrast enhancement and an infiltrative pattern. Thus, a scar is generally associated with a lower T2 signal, whereas a recurrent tumor exhibits an intermediate to high signal on T2-weighted images. MRI have low PPV and can overestimate the disease. MRI leads to false positive estimation of post-operative changes as recurrent disease in the present case as well.[6]

To increase the efficacy of MRI in differentiating recurrence from post treatment changes, the role of Diffusion-weighted MRI images (DWI) is promising.[6] DWI is based on the T2 sequence of MRI. The apparent diffusion coefficient (ADC) measures the degree of motion of water molecules and is thought to serve as a surrogate measure for tissue cellularity.

Residual or recurrent tumour, due to increased cellularity, typically produces a low ADC, whereas scar composed of large fibroblasts allowing more movement of water molecules results in a relatively higher ADC. Thus, DWI might have been valuable in this case. [6]

PET CT has distinct advantage as it offers information regarding the functional activity of the treated disease along with anatomical details. It is more sensitive than CECT, MRI, ultrasound, and physical examination in detecting recurrent disease.[1] Systematic review and meta-analysis by Gupta et al showed the role of PET/CT in response assessment and surveillance imaging of head and neck squamous cell carcinoma patients. The study reported a high negative predictive value (NPV) (>94%) and a low positive predictive value (PPV) (<60%) for both primary site and cervical nodes.

For patients with a PET-positive result, a biopsy is recommended because of a relatively high false-positive rate due to post-treatment inflammation.[4]

In the postoperative period, the first response of the human body in wound healing is the formation of granulation tissue from the connective tissue around the damaged area, which mainly contains inflammatory cells, fibroblasts, myofibroblasts, and small vessels. Over time, the granulation tissue disappears by apoptosis and is replaced by immature and then mature scars in the presence of macrophages, which take place within 2 months of injury.[2] During these initial few months, there is increased FDG uptake seen on PET/CT images, and the FDG uptake tends to decrease gradually over time as the inflammation subsides. Post-surgical anatomical distortion can further increase the diagnostic dilemma in such cases. A review of the literature, by Zimmer et al in 2005, recommended that PET imaging should not be performed before 2 to 3 months after the surgery or chemoradiation therapy to reduce the incidence of false-positive results secondary to inflammation.[5] Similarly, in our case postoperative Inflammation and Infection led to high FDG uptake in the post-operative sites even after 8 weeks of surgery.

The presence of a clinically suspicious lesion in buccal mucosa along with intense focal uptake of FDG raised the suspicion of recurrence in the present case. This focal uptake can be explained by the fact that localised infection of the bone and granulation tissue can lead to focal FDG uptake. The presence of inflammatory cells (eg, neutrophils, lymphocytes, macrophages) with increased metabolic activity result in increased activity on FDG PET. [9]

Stephanie et al in their study concluded that despite high false-positive rates of PET CT in the immediate postoperative period, it has the potential to prevent overly aggressive treatment thus reducing toxicity and treatment related cost. PET CT application can lead to more aggressive treatment when appropriate (loco-regional persistent or recurrent cancer) and can define radiation therapy treatment fields and doses. But, PET CT findings should be confirmed by biopsy as PET has a significantly high false-positive rate in the early postoperative period.[1]

The hypothyroid state of the patient could have contributed to high false positive values on PET CT and MRI. However, no relevant literature is available for the same. It warrants further research on the effect of hypothyroidism on PET uptake.

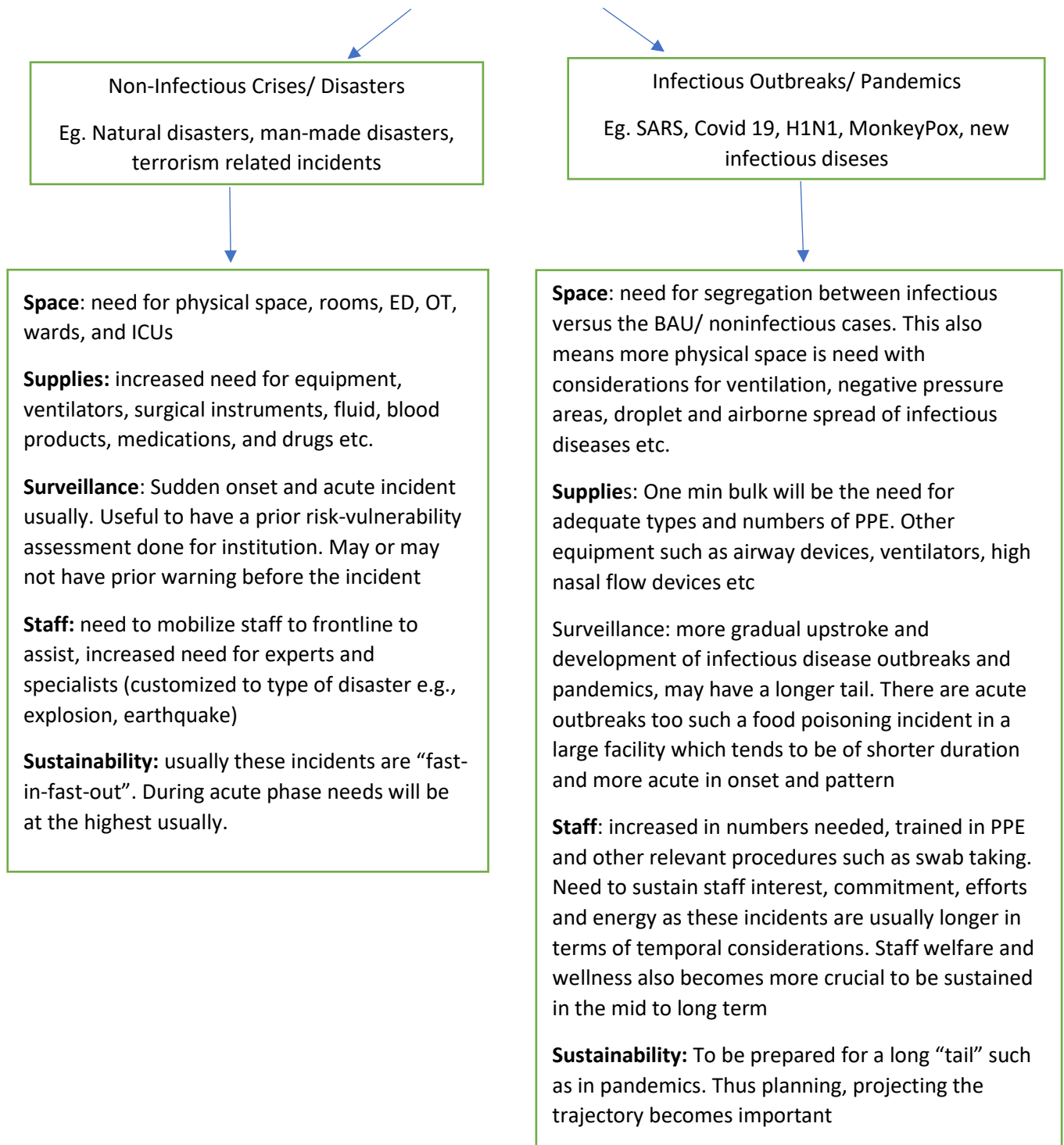
## Conclusion

PETCT is an important imaging modality in the post treatment surveillance of Head and neck cancers. However, accuracy of PET CT is limited in the early postoperative period due to post treatment changes. The accuracy improves moderately if performed more than 12 weeks of completion of treatment. The role of DWI needs to be explored further as it has shown promising results in differentiating recurrence and inflammation. A positive biopsy is confirmatory but a negative biopsy does not rule out disease. Moreover, there may be false-negative results due to granulation and fibrosis in the post operative period. A close follow up with thorough clinical examination and appropriate imaging is recommended in such cases.

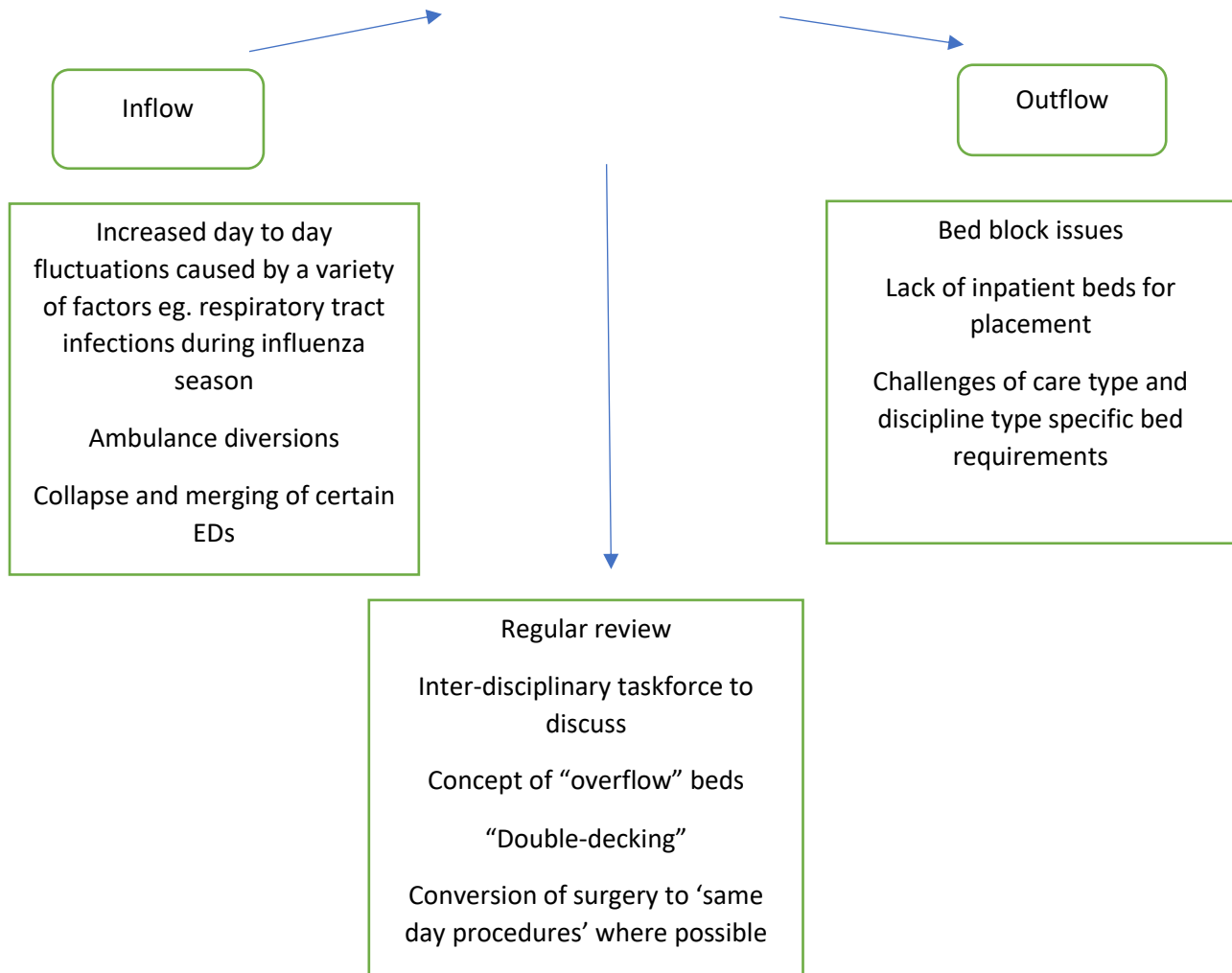
## References

1. Utility of PET/CT imaging Performed early after surgical resection in the adjuvant treatment planning for head and neck cancers; Stephani A. Shintani, M.D, Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 2, pp. 322–329, 2008
2. FDG-PET/CT in the Postoperative Period: Utility, Expected Findings, Complications, and Pitfalls ; Gunjan Garg, MD et al. ; seminars in nuclear medicine 2017
3. Isles MG, McConkey C, Mehanna HM. A systematic review and meta-analysis of the role of positron emission tomography in the follow up of head and neck squamous cell carcinoma following radiotherapy or chemoradiotherapy. Clin Otolaryngol 2008; 33:210–222
4. Gupta T, Master Z, Kannan S, et al: Diagnostic performance of post-treatment FDG PET or FDG PET/CT imaging in head and neck cancer: A systematic review and meta-analysis. Eur J Nucl Med Mol Imaging 38:2083-2095, 2011,
5. Zimmer LA, Branstetter BF, Nayak JV, et al. Current use of 18F-fluorodeoxyglucose positron emission tomography and combined positron emission tomography and computed tomography in squamous cell carcinoma of the head and neck. Laryngoscope 2005;115:2029–2034
6. Postoperative and Postradiation Head and Neck Role-of Magnetic Resonance Imaging, Andreea G. Moore, MD and Ashok Srinivasan, MD, Topics in Magnetic Resonance Imaging • Volume 24, Number 1, February 2015

7. Tomura N, Watanabe O, Hirano Y, et al. MR imaging of recurrent head and neck tumours following flap reconstructive surgery. Clin Radiol. 2002;57: 109–113
8. Accuracy of Ultrasonography-Guided Fine-Needle Aspiration in Detecting Persistent Nodal Disease After Chemoradiotherapy, Gitanjali M. Fleischman, MD 1; Brian D. Thorp, MD1; Megan Difurio, MD2; et al, JAMA Otolaryngol Head Neck Surg. 2016;142(4):377-382. doi:10.1001/jamaoto.2015.3934
9. Guhlmann A, Brecht-Krauss D, Suger G, et al. Chronic osteomyelitis: detection with FDG PET and correlation with histopathologic findings. Radiology 1998; 206:749 –754



**Fig 1:** Resilient Engineering Considerations in Non-Infectious (Disasters) versus Infectious Diseases (Pandemics) Incidents



**Fig 2:** Map of the Issues Encountered with Surge during “Business as Usual” Periods

## References

1. Wilder-Smith A, Law JGH. Risk of respiratory infections in healthcare workers: Lessons on infection control emerge from the SARS outbreak. South East Asian J Trop Med Pub Health 2005; 36(2): 481-488
2. Lateef F, Stawicki SP, Lee MX, Krishnan V, Sanjan A, Sinir FM et al. Infection control, in situ simulation and failure mode effect analysis to fine-tune the change management during Covid 19. Journal of Emergency, Trauma and Shock 2020; 13: 239-245
3. Tham KY. ED response to SARS: a prototype response to bioterrorism. Ann Emerg Med 2004; 43(1): 6-14

4. Lateef F. Handling Covid 19: minimizing our blindspots by using checklists and promoting collaborative culture. *J Qual Healthcare and Economics* 2020; 3(6): 000185
5. Friend Y. The challenge of emergency medicine facing the Covid 19 outbreak. *Eur J Emerg Med* 2020; 9546
6. Lateef F. The impact of Covid 19 pandemic on ED attendance: what seems to be keeping the patients away? *Journal of Emergency, Trauma and Shock* 2020; 13: 246-251
7. Lateef F. Through the ethical lenses: There is really more than meets the eye with Covid 19. *Archives of Emerg Med and Intensive Care* 2020; 3(10): 6-16
8. Lin M, Beliaevsky A, Katz K, Powis JE, Ng W, Williams V et al. What can early Canadian experience screening for Covid 19 teach us about how to prepare for a pandemic. *CMAJ* 2020; 192(12): E314-E318
9. Bunge EM, Hoet B, Chen L. The changing epidemiology of human monkey pox: a potential threat? A systematic review. *PLoS Negl Trop Dis* 2022; 16(2): e0010141
10. Simpson K, Heymann D, Brown CS et al. Human monkey pox : after 40 years: an unintended consequence of smallpox eradication. *Vaccine* 2020; 138(33): 5077-5081
11. Sasaki J, Shiino Y, Kato Y, Kudo D, Fujita M, Miyari I et al. Checklist for infection control in the ED. *Acute Med and Surgery* 2020; 7: e540
12. Pryashkevich AI, Melnikova IB. Feature of the designing of infectious diseases hospital in a pandemic. *Earth and Environmental Sciences* 2022; 988: 052066
13. Hoffman RR, Hancock P. Measuring resilience. *Human Factors* 2016; 59(4): 564-581
14. Woods DD. Essential characteristics of Resilience. In Hollnagel E, Woods DD, Leveson N (Eds) in *Resilience Engineering*, pp. 55-67. Aldershot UK, Ashgate, 2006
15. Woods DD. Four concepts of resilience and the implications for the future of emergency medicine. *Reliab Eng Supt Saf* 2015; 141: 5-9
16. Lateef F. Culture of psychological safety in the ED: Don't forget the hidden curriculum. *Archives of Emerg Med and Intensive Care* 2021; 4(1): 18-26
17. Zhang YH, Dutta A, Fook-Chong S, Johari NAB, Lee GT, Lateef F. Psychological safety in the ED during Covid 19 pandemic: a single centre survey study. *Clin Research in Emerg Med* 2020; 2(3): 1027

18. Therrien MC, Normandin JM, Denis JL. Bridging complexity theory and resiliency to decrease surge capacity in health systems. *J Health Org Manage* 2017; 3191): 96-109
19. Plsek PE, Greenhalgh T. The challenge of complexity in healthcare. *BMJ* 2001; 323: 625-628
20. Patel VL, Shidhaye R, Dev P, Shortliffe EH. Building resiliency in emergency medicine physicians: Anticipating the next catastrophe. *BMJ Health Care Inform* 2021; 28: e100343
21. Anderson JE, Ross AJ, Beck J. Beyond “find and fix”: improving quality and safety through resilient healthcare systems. *Int J Qual Healthcare* 2020; 32: 204-211
22. Son CW, Sasngohan F, Rao AH, Larsen E. Resilient performance of EDs: patterns, models and strategies. *Safety Sci* 2019; 120: 362-373
23. Bennett P, Hardiker NR. The use of computerized clinical decision support systems in emergency care: a substantive review of the literature. *J Am Med Informatics Assoc* 2016; 24: ocw151
24. Lateef F, Tan BKK, Yunus M, Mohammed AAR, Galwankar S, Al Thani H et al. BRAVE: a point of care adaptive leadership approach to providing patient-centric care in the ED. *Journal of Emergency, Trauma and Shock* 2022; 15: 47-52