

ORIGINAL ARTICLE

Evaluation of the Effect of Acquisition Time on Image Quality of Adrenal Carcinoma PET/CT Scans

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Abstract

Purpose: Adrenal adenomas are best detected and understood using a Positron Emission Tomography/Computed Tomography (PET/CT) scanner. When doing PET scans, the acquisition time of 18-Fluorodeoxyglucose (¹⁸FDG) absorption is crucial as it determines the diagnostic accuracy and quality of the images. This study aimed to investigate the effects of various acquisition periods to assess the efficacy of PET/CT in identifying adrenal adenomas (1.5 vs. 3 minutes).

Materials and Methods: The research included 30 patients who were thought to have adrenal adenomas. Following the ¹⁸FDG injection, PET/CT imaging was performed on each patient using one of two distinct acquisition times: 1.5 or 3 minutes. The image quality was objectively evaluated using a 5-point Likert scale. Experienced nuclear medicine professionals used consensus reading to assess diagnostic performance for adrenal adenoma identification.

Results: The preliminary findings showed that compared to the 1.5-minute acquisition technique, PET/CT imaging with a 3-minute duration after ¹⁸FDG injection produced considerably superior image quality ($p < 0.05$). In addition, the longer acquisition time significantly increased the chance of detecting the lesion more precisely, improving the visualisation and characterisation of adrenal adenomas. With greater sensitivity and specificity, the 3-minute acquisition methodology showed better diagnostic accuracy for adrenal adenoma identification than the 1.5-minute approach.

Conclusion: The study suggests that extending the acquisition time to 3 minutes improves image quality and diagnostic performance for adrenal adenoma detection, potentially improving patient care by facilitating accurate diagnosis and treatment planning.

Keywords: Positron Emission Tomography/Computed Tomography; Adrenal Cancer; Acquisition Time; Image Quality.

1. Introduction

"Incidentalomas" refer to the adrenal lesions found by chance in as much as 5% of cross-sectional exams conducted for other reasons. Depending on their function, adrenal lesions may be either benign or cancerous. Overproduction of hormones or metabolites indicates a functional adrenal lesion, while an enlarged adrenal gland without excessive hormone production indicates a nonfunctioning lesion. There are two types of adrenal lesions: benign and malignant. Benign tumours might be functional or non-functional. On the other hand, nonfunctioning adrenal lesions account for around 5% of all abdominal CT scans. A thorough study of adrenal hormones may assist in determining the adrenal function and the kind of hormonal hypersecretion that may develop after discovering an adrenal mass [1–3].

Comparative CT scans of the abdomen and thorax often reveal the adrenals. Because of its extensive usage and excellent spatial and temporal resolution, CT is usually the first imaging modality that discerns adrenal lesions. With unenhanced acquisition, density assessment and lesion measuring may be done with pinpoint accuracy. When there is diagnostic doubt, an accurate diagnosis may be attained using a multiphasic acquisition strategy [4,5]. Utilizing computed tomography allows for the planning of cancer treatment, staging of the illness, and guidance of a needle biopsy, among other applications (CT). Particularly helpful in diagnosing adrenal adenomas and identifying various tissue components in inhomogeneous lesions, Magnetic Resonance Imaging (MRI) plays a crucial role in adrenal lesion characterization due to its high-contrast resolution and inherent tissue characterization ability [6].

Finally, functional imaging may be a diagnostic process in certain circumstances. Combining morphological and functional imaging using Fluorodeoxyglucose (FDG) PET-CT helps to differentiate between benign and malignant adrenal lesions on time. Elevated tissue metabolism precedes anatomical changes in most malignant tumors. When the absorption of FDG by the adrenal glands is more significant than that by the liver, it is considered malignant. The overlap can result in a wrong diagnosis since the typical adrenal SUV_{max} range is 0.95–2.46, whereas the usual liver SUV_{max} range is 1.5–2.0. This

issue has been addressed by proposing the adrenal/liver SUV ratio to distinguish benign from malignant tumours [7,8]. The two disadvantages of PET scans include the inability to distinguish between benign and malignant lesions and the difficulty in identifying initial tumours that are not FDG-avid (i.e., tumours that do not uptake the tracer used in PET scans) [9].

PET using ^{18}F -FDG has emerged as a well-established and sensitive method for delivering quick, comprehensive, and reliable information in oncology, cardiology, and neurology. Nevertheless, PET/CT scans may still take a while, and getting good enough images can be complex, especially with younger patients, those with orthopaedic conditions, and those with smaller heads. Misalignment might occur due to patient movement without efficient positioning devices. To alleviate a patient's discomfort or anxiety, the staff is often compelled to enter the examination room, where they are exposed to unwanted radiation while adjusting the patient's setting or calming them down. Therefore, decreasing the scanning duration may improve patient comfort and the examination's cost-effectiveness [10–14].

Typically, improved spatial resolution is achieved with longer acquisition times, allowing a more significant number of coincidental radioactive decays to be recorded. Research using phantom scanners has shown that a substantial improvement in lesion detection rate may be achieved with minimal improvements to signal-to-noise ratio and lesion contrast [15]. In agreement with this study, Hausmann *et al.* [16] conducted a study to determine an acceptable minimum acquisition time in tumour diagnoses by PET/CT. They found that lowering scanning time below 3 minutes per bed position adversely affects lesion detection rates and maximum standardized uptake value (SUV_{max}) [17,18].

So, this study aimed to evaluate the effectiveness of the acquisition time of ^{18}F FDG for patients with adrenal carcinoma, whether it is 1.5 or 3.0 minutes, and assess its effect on image quality for cancer staging.

2. Materials and Methods

This is a retrospective clinical study with consecutive sampling techniques conducted in the Baghdad Center of Radiation Therapy and Nuclear Medicine from January 2023 to October 2023. Thirty patients with adrenal carcinoma were involved in this study. Diabetic patients, pregnant women, and patients with blood glucose levels higher than 180 mg/dL were excluded from the study. Patients with benign tumors or chronic diseases were excluded from this study. Informed written ethical consent was taken from each patient.

Patients underwent fasting for at least 8 hours before administering ^{18}F FDG, with a dose of 300 MBq allocated per 70 kg of body weight. Blood glucose analysis was conducted for each subject. The mean uptake phase length was 82 minutes (with a range of 55 to 130 minutes) for an acquisition time of 3 minutes, and the phase length was 90 minutes (with a range of 51 to 148 minutes) for 1.5 minutes. The PET/CT with a 4D CT scan device is manufactured by GE, USA. Featuring a specific resolution of 5.0 mm. Eight-bed positions were used for the whole-body PET scan, spanning from the skull to the mid-thighs. The CT settings are primarily configured at 120 kVp, a pitch value of 0.8, and 50 mA, with a collimator width of 1.2 mm. Three detector rings with a 16-centimeter axial coverage were utilized in this investigation. The CARE Dose4D system, which adapts the radiation dosage based on the patient's dimensions, was used to get a low-dose helical CT scan while the patient breathed shallowly. Randomization was used to determine the sequence of the PET scans, which were conducted from the mid-thigh. The first step was to conduct a 3-minute scan for each bed position. This study used contrast-enhanced and body weight-adjusted iodinated intravenous contrast medium for each patient.

Patients previously diagnosed by CT with metastasis, with no further contrast-enhanced imaging procedures. The attenuation-corrected CT's radiation dosage was raised to 80 mA to achieve satisfactory image quality. Each patient only needed a single attenuation-corrected CT scan for both PET acquisitions. All PET/CT scans were reviewed by a board-certified nuclear medicine expert and a first-year nuclear medicine resident at a workstation with

fusion with reconstruction method options inside the software PET/CT. The reconstruction is often an iterative procedure using Ordered Subset Expectation Maximization (OSEM) with Time-of-Flight (TOF) and Point Spread Function (PSF) for increasing resolution and lesion contrast. Scans performed include a matrix up to 128×128 , voxel size of 2.5 mm^3 , and achieving uniformity, using sequences from 4 iterations with 32 subsets to reduce noise and optimize acquisition. For attenuation, scatter, and random event corrections, genuinely accurate CT data are utilized.

Image quality was assessed using a 5-point Likert scale, ranking from best to worst. 1. Outstanding, 2. Acceptable, 3. Moderate, 4. Poor, 5. Very poor. Lesions were identifiable. The participants' perception of the photos constituted the foundation for the quality evaluation.

The statistical analysis was performed using SPSS version 28.0. The results were considered significant if the p-value was ≤ 0.05 , which suggests that there is less than a 5% possibility of achieving the results observed at random.

3. Results

Table 1 presents the characteristics of cancer patients in this study, including sex, age (in years), and tumor size (in centimeters). The analysis shows no significant difference in age and tumour size between those scanned with an acquisition time of 1.5 min and 3.0 min. A comparison was performed of sex with an acquisition time of 1.5 minutes and 3.0 minutes. The prevalence of males was higher than females. Males in the group were 63%, while females were 37% within the group, with the acquisition time taken being 1.5 minutes. On the other hand, in the group with an acquisition time of 3.0 minutes, the gender distribution is relatively evenly spread, where males were 53% while females were only 47%.

The maximum standardised uptake value (SUV_{max}) and density of adrenal mass in the Hounsfield Unit (HU) were assessed for both acquisition time groups. The statistical analysis shows a significant difference in SUV_{max} between the patients scanned with a 3.0 min acquisition time and those with a 1.5 min acquisition time. There was no significant difference in the HU

Table 1. Characteristics of adrenal carcinoma in metastasis patients

	1.5 Minutes	3.0 Minutes	<i>p</i> -value
Age (Years)	56.03 ± 11.29 (32 – 72)	60.23 ± 9.71 (34 – 84)	0.1280
Tumor Size (cm)	4.54 ± 1.31 (2 – 6.9)	4.79 ± 1.52 (2 – 7.1)	0.5090
Sex	Male 19 (63.33%) Female 11 (36.67%)	Male 16 (53.33%) Female 14 (46.67%)	
* Significant Difference at <i>p</i> -value ≤ 0.05.			

Table 2. The standardised uptake value (SUV) and density (HU) of adrenal mass

		1.5 Minutes	3.0 Minutes	<i>p</i> -value
SUV _{max}	Mean	14.6	15.3	0.0422*
	SD	4.01	3.94	
	Range	(3.2 – 30.31)	(3.9 – 43.12)	
Density Hounsfield Unit (HU)	Mean	31.35	35.93	0.0585
	SD	8.91	7.03	
	Range	(18.12 – 45.20)	(19.75 – 51.46)	
* Significant Difference at <i>p</i> – value ≤ 0.05.				

values between those scanned for 3.0 min and those scanned for 1.5 min.

Two experienced specialists in nuclear medicine assessed the image quality using five points of the Likert Scale, as presented in Table 3. It was shown that most patients were classified as having excellent image quality, followed by good and intermediate image quality. A higher percentage of patients was observed for those with an acquisition time of 3.0 minutes than for those with 1.5 minutes. No poor image quality was observed for patients who scanned with an acquisition time of 3.0 minutes, other than those with 1.5 minutes.

Table 3. Comparison of Acquisition time in Image Quality using a 5-point Likert Scale

Rating	1.5 Minutes	3.0 Minutes
1 (Outstanding)	19 (63%)	22 (73%)
2 (Acceptable)	5 (17%)	6 (20%)
3 (Moderate)	4 (13%)	2 (7%)
4 (Poor)	2 (7%)	0
5 (Very poor)	0	0
1. Excellent Image Quality, 2. Good Image Quality, 3. Intermediate Quality, 4. Poor Image Quality, 5. Very Poor Image Quality		

4. Discussion

The research presented here shows that using advanced 3D high-definition PET/CT scanners could significantly reduce acquisition times per bed position from 3 minutes to 1.5 minutes, making it clinically feasible. Lesion identification rates were consistent, even among less experienced observers, and the reduced collection duration only slightly compromised image quality.

The demographic features of metastatic patients, including age, tumour size, and sex distribution were consistent across the acquisition time groups of 1.5 minutes and 3.0 minutes. This standardization ensures that any variations in quantitative measurements and image quality are mostly due to changes in acquisition time rather than patient-specific factors.

The results showed that patients with a 3.0-minute acquisition time had significantly higher SUV_{max} values than those scanned with a 1.5-minute acquisition period. The 3.0-minute group stood out with higher SUV_{max} values. This data implies that the adrenal masses absorb more tracer with longer acquisition durations, which might make PET imaging

more sensitive to metabolic activities linked to metastases.

Although no statistically significant difference existed between individuals examined with an acquisition period of 3.0 and 1.5 minutes, the HU measures of adrenal masses were more significant in the former group. The absence of statistical significance indicates that other variables, such as tumor heterogeneity or scanner configurations, may affect HU variations rather than extended acquisition durations, hence improving CT image quality and HU assessments.

Results from the Likert Scale assessment of image quality were similar across the two groups of acquisition times. The image quality for most patients was deemed exceptional, with excellent and intermediate quality following closely behind. Notably, the 3.0-minute acquisition group had no cases of poor image quality, but a tiny percentage of patients scanned with 1.5 minutes had worse evaluations for image quality. It seems that the quality of the images is increased with longer acquisition times, which might lead to more confidence and accuracy in diagnostics.

The findings of this study have important impacts on clinical practice. Optimizing acquisition settings to enhance diagnostic value is crucial, as shown by the variations in SUV_{max} and image quality between the 1.5-minute and 3.0-minute acquisition groups. Acquiring images for extended periods improves image quality and increases SUV_{max} values, making identifying and characterizing metastatic adrenal lesions easier. These findings support the notion that PET/CT imaging protocols should include extended acquisition times for patients with potential adrenal metastases, enhancing diagnostic accuracy and overall patient outcomes. This means that an increase in acquisition time has a more positive influence on the detection of metastasis than non-metastatic cases.

There has been no assessment of the clinical significance of the results of phantom investigations, which indicates that lesion detection rates may be significantly increased with minimal changes in objective imaging parameters. For instance, according to Farquhar *et al.* [19], in vitro results, the variation of the contrast-to-noise ratio was most significantly predicted by the scan time. To get better contrast-to-

noise ratios, they demonstrated that scanning for an additional 1–4 minutes for each bed position was the most successful. The scientists discovered that a less than twofold contrast enhancement was sufficient to transform detection performance from subpar to outstanding while imaging a thorax phantom with three different-sized spheres to represent lesions (0.45, 1.0, and 1.9 mL).

Brown *et al.* [17] in vitro and in vivo studies corroborate these results. Under circumstances of shortened acquisition time, they found a tendency toward fewer lesions, based on quantitative and qualitative analysis of 3-dimensional ^{18}F -FDG phantom and patient PET scans. Various periods (1, 2, 3, 4, and 5 minutes) were used to obtain phantom images with varying lesion-to-background contrast ratios. The patient data was acquired using list-mode collection to get comparable 2-, 3-, and 4-minute frames. Qualitative and quantitative research revealed that image quality degraded below the 4-minute capture frames in phantom and patient images. Among the patient photos, one lesion in a 4-minute acquisition wasn't picked up in a 3-minute acquisition, and four other lesions were missed in 2-minute imaging. The authors concluded that typical 3-dimensional-mode ^{18}F -FDG imaging should not have an acquisition time frame lower than 3 minutes. More research is required to determine the clinical significance of the result; however, only five patients were included in the PET scans.

Contrary to earlier assumptions, our findings raised doubts about the significance of these in vitro findings for cancer diagnostic imaging. Thus far, our clinical research on PET/CT image quality and acquisition times seems to have reported the most significant patient cohort. A previous investigation by Farquhar *et al.* and a more recent clinical trial by Goethals *et al.* corroborated our findings [19]. Researchers showed that visual identification of malignant tumours in the head and neck area was unaffected by decreasing image quality while evaluating 17 patients with head and neck cancer using acquisition periods ranging from 10 to 0.5 minutes.

The high-definition PET technology our PET scanner uses is based on sophisticated iterative reconstruction methods that have been on the market since 2007. Perhaps our findings were influenced by

this technological advancement and the much-increased tracer absorption in cancerous lesions [15].

Consistent with the work by Goethals *et al.* [20], our findings indicate that the two scan durations may be semi-quantitatively compared for ^{18}F -FDG uptake. An SUV's ability to differentiate between benign and malignant tumours and track treatment efficacy makes this finding crucial. Size might also significantly affect radiation oncology treatment planning using PET imaging. To ensure that the radiation dosage reaches the tumour while minimizing it to healthy tissue, precise volume delineation of the target is essential [21,22]. According to our data, the observed PET/CT volumes were unaffected by the acquisition time. However, there was a slight change in the lesion size according to the acquisition time; after 1.5 minutes, the size increased somewhat. One possible explanation for this observation is that less accidental radioactive decay occurs at shorter acquisition times, leading to a more significant blurring at 1.5 minutes [22,23].

The minimal interobserver variability is another essential factor that gives PET/CT its tremendous relevance in tumour staging. It is true that when defining the gross tumour volume using CT scans, there is much room for observer variability. Using coregistered ^{18}F -FDG PET scans often yields a more uniform gross tumour volume definition [24]. There is no interobserver variance when calculating the SUV_{max} of lung nodules, according to a review that examined the interobserver variability of SUV_{max} and SUV_{mean} readings on ^{18}F -FDG PET/CT scans in patients with localized pulmonary lesions [25].

Additional technological advancements will undoubtedly contribute to even faster scanning times. With recent technological advancements, including a wider Region Of Interest (ROI), a 4-detector ring system, and time-of-flight technology, the time it takes to do a full body scan might be drastically reduced [26]. With each response line having its time bin, the time-of-flight projections can provide a less hazy and more accurate estimation of the real image. We need further research in the future to determine how well these technological advancements worked.

Bear in mind that this research has several caveats, such as a small sample size and the fact that it is retrospective in nature. Image quality and quantitative

measures in metastatic adrenal lesions should be better understood if future studies investigate how different acquisition settings, such as reconstruction methods and image processing approaches, affect these variables.

5. Conclusion

We conclude that acquisition time is critical for assessing metastatic adrenal masses in PET/CT imaging. A longer acquisition time was linked to better image quality, increased diagnostic confidence, and higher SUV_{max} values. These results highlight the need for fine-tuning acquisition settings to provide the best possible PET/CT imaging results for patients suspected of having adrenal metastases. Even for less experienced observers, our findings show that acquisition periods may be shortened without affecting the lesion identification rate in various tumour entities. However, at 1.5 minutes, the less experienced observer assessed the image quality somewhat poorer. Based on our past experiences, we would exercise caution when attempting to decrease acquisition time in patients who are overweight or have elevated blood sugar levels, especially in vital areas like the upper abdomen.

References

- 1- Tarallo M, Crocetti D, Fiori E, Sapienza P, Letizia C, De Toma G, *et al.* "Criticism of the learning curve in laparoscopic adrenalectomy: A systematic review." Vol. 171, *Clinica Terapeutica*, (2020).
- 2- Ungureanu S, Şipitco N, Alexa Z, Gonța V, Bujac M, Parnov M, *et al.* "MEN 2A syndrome – Multiple endocrine neoplasia with autosomal dominant transmission." *Int J Surg Case Rep*;73, (2020).
- 3- Pedullà G, Crocetti D, Paliotta A, Tarallo MR, De Gori A, Cavallaro G, *et al.* "Surgical treatment of pheochromocytoma in MEN 2." *Ann Ital Chir*;85(5), (2014).
- 4- Guerrisi A, Marin D, Baski M, Guerrisi P, Capozza F, Catalano C. "Adrenal Lesions: Spectrum of imaging findings with emphasis on multi-detector computed tomography and magnetic resonance imaging." *J Clin Imaging Sci*, 3(1), (2013).
- 5- Mete O, Erickson LA, Juhlin CC, de Krijger RR, Sasano H, Volante M, *et al.* "Overview of the 2022 WHO Classification of Adrenal Cortical Tumors." Vol. 33, *Endocrine Pathology*, (2022).

- 6- Gunna S, Neyaz Z, Bhatia E, Marak RS, Mishra R, Verma R. "Results of percutaneous computed tomography-guided biopsy of adrenal lesions and spectrum of computed tomography findings." *J Clin Imaging Sci.*;10(1), (2020).
- 7- Caoili EM, Korobkin M, Brown RKJ, Mackie G, Shulkin BL. "Differentiating adrenal adenomas from non-adenomas using ¹⁸F-FDG PET/CT: quantitative and qualitative evaluation." *Acad Radiol.*;14(4):468–75, (2007).
- 8- Sahdev A. "Imaging incidental adrenal lesions." *Br J Radiol* [Internet]. 20;96(1141):202–18, (2022) Available at: <https://doi.org/10.1259/bjr.20220281>
- 9- Abdel Razek AAK, Sadek AG, Kombar OR, Elmahdy TE, Nada N. "Role of apparent diffusion coefficient values in differentiation between malignant and benign solitary thyroid nodules." *American Journal of Neuroradiology*;29(3), (2008).
- 10- Shinya T, Rai K, Okumura Y, Fujiwara K, Matsuo K, Yonei T, et al. "Dual-Time-Point F-18 FDG PET/CT for Evaluation of Intrathoracic Lymph Nodes in Patients with Non-Small Cell Lung Cancer." *Clin Nucl Med.*;34(4), (2009).
- 11- Lan XL, Zhang YX, Wu ZJ, Jia Q, Wei H, Gao ZR. The value of dual time point 18F-FDG PET imaging for the differentiation between malignant and benign lesions. *Clin Radiol.* (2008);63(7).
- 12- Arena V, Skanjeti A, Casoni R, Douroukas A, Pelosi E. "Dual-phase FDG-PET: delayed acquisition improves hepatic detectability of pathological uptake." *Radiol Med.*;113(6), (2008).
- 13- Tokariev M, Vuontela V, Perkola J, Lönnberg P, Lano A, Andersson S, et al. "A protocol for the analysis of DTI data collected from young children." *Methods X.*;7, (2020).
- 14- Beyer T, Antoch G, Müller S, Egelhof T, Freudenberg LS, Debatin J, et al. "Acquisition protocol considerations for combined PET/CT imaging." Vol. 45 Suppl 1, *Journal of Nuclear Medicine: official publication, Society of Nuclear Medicine*, (2004).
- 15- Jones T, Townsend D. "History and future technical innovation in positron emission tomography." *Journal of Medical Imaging.*;4(1), (2017).
- 16- Hausmann D, Dinter DJ, Sadick M, Brade J, Schoenberg SO, Büsing K. "The impact of acquisition time on image quality in whole-body 18F-FDG PET/CT for cancer staging." *J Nucl Med Technol.*;40(4), (2012).
- 17- Brown C, Dempsey MF, Gillen G, Elliott AT. "Investigation of 18F-FDG 3D mode PET image quality versus acquisition time." *Nucl Med Commun.*;31(3), (2010).
- 18- Goethals I, D'Asseler Y, Dobbeleir A, Deblaere K, Ham H. "The effect of acquisition time on visual and semi-quantitative analysis of F-18 FDG-PET studies in patients with head and neck cancer." *Nucl Med Commun.*;31(3), (2010).
- 19- Farquhar TH, Llacer J, Sayre J, Tai YC, Hoffman EJ. "ROC and LROC analyses of the effects of lesion contrast, size, and signal-to-noise ratio on detectability in PET images." *Journal of Nuclear Medicine.*;41(4), (2000)
- 20- Goethals I, D'Asseler Y, Dobbeleir A, Deblaere K, Ham H. "The effect of acquisition time on visual and semi-quantitative analysis of F-18 FDG-PET studies in patients with head and neck cancer." *Nucl Med Commun.*;31(3), (2010).
- 21- Alqahtani MM, Willowson KP, Constable C, Fulton R, Kench PL. "Optimisation of 99mTc whole-body SPECT/CT image quality: A phantom study." *J Appl Clin Med Phys.*;23(4), (2022).
- 22- Akin EA, Washington G. "Optimizing Oncologic FDG-PET/CT Scans to Decrease Radiation Exposure." *Image Wisely: Radiation Safety in Adult Medical Imaging.* (2017).
- 23- He Y, Gu Y, Yu H, Wu B, Wang S, Tan H, et al. "Optimising acquisition times for total-body positron emission tomography/computed tomography with half-dose 18F-fluorodeoxyglucose in oncology patients." *EJNMMI Phys.*;9(1), (2022).
- 24- Toya R, Matsuyama T, Saito T, Imuta M, Shiraishi S, Fukugawa Y, et al. "Impact of hybrid FDG-PET/CT on gross tumor volume definition of cervical esophageal cancer: Reducing interobserver variation." *J Radiat Res.*;60(3), (2019)
- 25- Woo MJ, Lowe SC, Devane AM, Gimbel RW. "Intervention to Reduce Interobserver Variability in Computed Tomographic Measurement of Cancer Lesions Among Experienced Radiologists." Vol. 50, *Current Problems in Diagnostic Radiology*, (2021).
- 26- Rao JS, Festoff BW, Baker JB, Morantz RA, Kimler B, Evans R. "Serpine Inhibitors of Urokinase and Thrombin in Normal Rat Brain and the 9L Brain Tumor: Evidence for Elevated Expression of Protease Nexin I-like Inhibitor and a Novel Sodium Dodecyl Sulfate-activated Tumor Antithrombin." *Cancer Res.*;50(16), (1990).