Transforming the stroke care continuum together

DAVID GOLAN[1], ALEJANDRO TOMASELLO WEITZ[2], STEFAN KIECHL[3]

[1] Co-founder and Chief Technology Officer at Viz.ai, Tel Aviv, Israel

[2] Vall d'Hebron Hospital, Barcelona, Spain

[3] Medical University of Innsbruck, Innsbruck, Austria

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Meeting summary/Abstract

This article is based on a symposium that took place during the European Stroke Organisation Conference (ESOC) 2021 and was sponsored by Medtronic. Four experts presented innovative technologies and concepts that could transform stroke care and improve patient outcomes. The technologies include an intelligent care coordination system, the artificial intelligence Software called Viz.ai, and a catheter tip distensibility concept based on effective inner diameter that could positively impact direct aspiration first pass thrombectomy results. The clinical section includes updates on the latest studies and guideline recommendations for risk stratification of patients, atrial fibrillation monitoring, stroke prevention and symptom control.

KEYWORDS: ARTIFICIAL INTELLIGENCE, ATRIAL FIBRILLATION, CATHETERS, CRYPTOGENIC STROKE, RECANALISATION

Corresponding author: David Golan - david@viz.ai

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The future is now, bringing AI to stroke care

David Golan

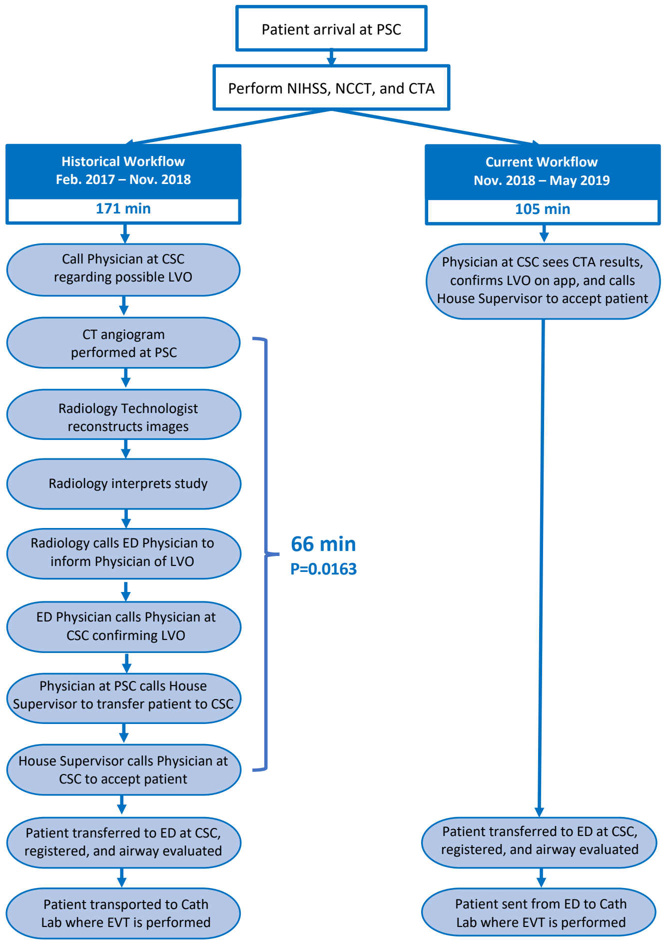
The treatment efficacy of endovascular treatments is highly time-dependent and delays due to logistics and communication problems are common.[1-3] The Viz.ai Platform is an FDA approved parallel workflow tool and intelligent care coordination system that allows the entire medical team to stay informed simultaneously, resulting in faster decisions and treatments for patients.[1,4] It consists of several parts:

- Artificial intelligence (AI) powered alerts for suspected large vessel occlusion (LVO) and intracerebral haemorrhage through a mobile app (every on-call staff member is automatically alerted and 92% of alerts are reviewed by the intended specialist within 5 minutes)[4]
- Advanced mobile image viewing (three dimensional (3D) manipulation, dynamic scrolling in all orientations, and CTP motion artifact correction)[4]
- Real-time patient information (scoring and patient updates, and stroke specific clinical information)[4]
- Secure communication (pictures and video sharing, and in-house stroke alert coordination)[4]

Evidence-based technology

A retrospective study of patients with LVO (N=43) compared the transfer time from a primary stroke centre (PSC) to a comprehensive stroke centre (CSC) before and after Viz.ai was implemented. Pre-Viz.ai, the workflow was serial: patients were admitted, scans were performed, and there was an escalation process involving many stakeholders including the CSC physician until a decision was made to transfer for treatment at the CSC. Once Viz.ai was installed, the workflow changed: the CSC physician received the computed tomography angiography (CTA) from the PSC, confirmed the suspected LVO in the app, and called the house supervisor to accept the patient at the CSC for treatment (Figure 1). There was a significant reduction in mean transfer time from 171 minutes (pre-Viz.ai) to 105 minutes (post-Viz.ai) with 66 minutes saved (P=0.0163), and the median hospital length-of-stay from admission to discharge decreased from 9.7 days to 7.2 days (P=0.0324).[1]

Figure 1. Workflow before and after the implementation of Viz.ai reproduced from Hassan et al.[1]



Another recent retrospective, real-world study collected data from 2544 patient scans across 139 sites (73, PSCs; 34, CSCs; 32, other). The sensitivity and specificity of the AI Software Viz.ai were high at 96.32% and 93.83% and the median time-to-notification of an LVO alert to the stroke team was 5 minutes and 45 seconds. In addition to different types of hospitals, this study evaluated the performance of the system while using a wide range of imaging models, technical skills, and diverse patient demographics.[5]

How Viz.ai works

Viz.ai utilises deep learning, a technology that emerged in the last 5–10 years and outperforms other algorithms due to human-like capabilities in many tasks that computers did not perform well before (perception and cognitive tasks, understanding images and text). As in the human brain, the basic units are artificial neurons wired together and structured in layers. They collect inputs that are assigned weights, and if they cross a certain threshold, they fire a signal. This structure can develop very abstract learning mechanisms to leverage LVO detection. Other innovations within Viz.ai are semantic segmentation, motion correction, and 3D rotation and modelling which allow the algorithm to detect more distal and partial occlusions.[4]

The workflow starts when Viz.ai receives a CT image which is uploaded to cloud storage. Basic operations such as stripping away the skull and aligning the scan are then performed, feeding it into two neural networks; one segments the MCA, and the other creates a full 3D model of the brain vasculature. These images are combined and analysed. If the algorithm decides the imaging qualifies as a suspected LVO, then Viz.ai generates an alert for immediate attention, facilitating communication and treatment.[4]

Catheter tip distensibility can influence aspiration force

Alejandro Tomasello Weitz

Complete revascularisation with a single device pass, the first pass effect (FPE), should be the primary goal of mechanical thrombectomy.[6] FPE is preferred because multiple passes prolong procedures, damage the endothelium, and potentially reduce efficacy and safety.[6,7] Retrospective data show a linear association between device passes and good functional outcomes which diminish as passes are repeated. Also, modified Rankin scores (mRS) of ≤2 were 61.3% vs 35.3% in FPE vs non-FPE patients, respectively and median time to revascularisation was 34 vs 60 minutes (P=0.0003) showing FPE independently predicts good clinical outcomes.[6] Specialists at Vall d'Hebron Hospital use a combined technique working with aspiration catheters and stent retrievers to achieve FPE, improve quality of recanalisation, understand the interaction between the clot and device, and achieve homogeneous results within the team.

Factors associated with aspiration force

Aspiration force depends in part on the vacuum system used. For example, the Penumbra Jet Engine pump produces the most significant aspiration force (28.8 inches Hg), while other devices generate a force similar to a 60 cc vacuum syringe (26.5–26.8 inches Hg).[8] Another important factor is the flow curve which is steady with the pump and falls early with the syringe.[9] The inner diameter (ID) of the catheter tip is an influential factor as well.[8] The effect of proximal flow arrest is not yet completely understood, but it may have a positive impact on getting faster and better quality recanalisation and outcomes by blocking antegrade flow, reducing distal fragmentation, reducing trans-clot pressure gradient, inversing Circle of Willis flow, and protecting neural tissues.[10,11] In addition, angles of interaction between the aspiration catheter and the clot of ≥125.5° are more effective (P=0.001).[12] Lastly, regarding catheter diameter, the R[4]Q aspiration catheter designed to maximise lumen and flow while minimising pressure loss increases aspirated flow rates and suction force compared to tubular designs. As the flow rate increases more in the smallest vessels, the device may improve embolectomy in narrow and distal vasculature.[13]

Moreover, the specialists at Vall d'Hebron Hospital noticed that some catheters used for direct aspiration first pass thrombectomy (ADAPT) would capture the clot better than others, so they conducted a study to evaluate the aspiration performance of catheters and the role played by distensibility and the thrombus-catheter tip interaction. They compared different catheters in a 3D printed carotid artery model and measured aspiration force (aspF) and distensibility to calculate the effective ID (eff-ID) that represents distensibility. Remarkably, the effID results indicated that the React 71 catheter had the highest aspF (it was not the catheter with the largest ID) (Table1). React 71 had a good relationship between ID and aspF (Pearson coefficient, r=0.9601), but it was better between aspF and distensibility (Pearson coefficient, r=0.9944). The investigators concluded that effID is a better parameter to estimate aspF than the manufacturer's ID and that catheter tip distensibility can positively impact ADAPT thanks to the tip's mechanical flexible behaviour.[14]

Latest topics in patient selection for monitoring and risk stratification

Stefan Kiechl

Causes of stroke – ESUS

The main causes of stroke are microangiopathy, macroangiopathy, cardiac embolism, rare causes, and cryptogenic stroke or embolic stroke of undetermined sources (ESUS). The sources of emboli in a proportion of ESUS cases include cancer (5–10% of ESUS by PET-CT); retrograde aortic embolism; and importantly, occult atrial fibrillation (AF)

Table 1. Aspiration force and catheter tip mechanical behaviour analysis. Reproduced from Li et al.[14]

Catheter	labID (in)	Experimental AspF ± SD (mN)	Theoretical AspF (mN)	Force	ID	effID (in)
5 MAX	0.054	218.62 ± 4.66	132.60	64.88	17.93	0.064
Sofia 5F	0.055	224.06 ± 7.53	137.55	62.89	16.32	0.064
Cat 6	0.060	286.65 ± 5.28	163.70	75.11	17.95	0.071
React 68	0.068	373.65 ± 14.18	210.26	77.71	19.12	0.081
ACE 68	0.068	338.10 ± 5.69	210.26	60.80	16.08	0.079
Cat 7	0.068	382.23 ± 5.26	210.26	81.79	18.83	0.081
Sofia Plus	0.070	392.21 ± 12.27	222.81	76.03	18.53	0.083
React 71	0.071	455.43 ± 9.67	229.22	98.68	24.76	0.089
Jet 7	0.072	396.75 ± 9.49	235.72	68.31	14.69	0.083

AspF, aspiration force; effID, effective inner diameter; ID, inner diameter; in, inches; labID, laboratory inner diameter; mN, millinewton; SD, standard deviation.

detectable with long-term monitoring in 29.1% of all ESUS patients.[15]

Also, atherosclerosis and AF are closely related; the risk factors of atherosclerosis except for LDL cholesterol are also risk factors for AF. Accordingly, small vessel disease, large vessel disease, and AF are expected to coexist.[16]

The challenge of AF and stroke

It is important to identify AF as these patients have a five-fold higher risk of stroke, twice the risk of dementia[17], a high risk of recurrent strokes, and more severe strokes. Regarding dementia risk, a large retrospective study (N=444,106) found that patients using oral anticoagulants (OACs) had 29% less risk of dementia than those who were not on OACs (HR, 0.71; 95% CI, 0.68–0.74).[18] On the other hand, there are highly effective stroke preventive measures such as direct oral anticoagulants (DOACs) and left atrial appendage occlusion (LAAO). LAAO is an alternative to DOAC, but a recent study showed that it can also be a valuable add-on to anticoagulants. In this study, LAAO was performed during standard heart surgery in patients with AF on anticoagulants and resulted in reduced stroke or systemic embolism in the LAAO group vs the non-LAAO group (4.8% vs 7.0%, respectively; HR, 0.67; 95% CI, 0.53–0.85; P=0.001).[19]

Guideline recommendations and recent studies

- The American Heart Association/American Stroke Association (AHA/ASA) Guideline from 2014 recommended prolonged AF monitoring (30 days) within 6 months of stroke (Class IIa) for patients with cryptogenic stroke or transient ischaemic attacks (TIA)[20]

- The European Society of Cardiology (ESC) Guidelines from 2016 recommend screening AF post-stroke and post-TIA continuously for 72 hours (Class I) and to consider long-term monitoring with non-invasive ECG monitors or implanted loop recorders to detect silent AF (Class IIa)[21]

- The focused update of the AHA criteria from 2019 added that implantable devices such as loop recorders are recommended to detect silent AF if external monitoring is inconclusive (Class IIa)[22]

A systematic review found that AF diagnostic yields vary from ECG (7.7%), to Holter (10.7%), and long-term monitoring

Table 2. Recent studies showing frequency of detected AF.[24-26]

Study	Monitoring	N	Age (mean years)	Inclusion window	Frequency of detected AF (number (%) needed to screen)
EMBRACE	30-day event recorder vs 24-hour Holter ECG	572	73 ± 9 [≥55]	<6 months	**16.1%** vs 3.2% after 30 days
CRYSTAL-AF	Implantable event recorder vs "standard"	441	61 ± 11 [≥40]	<3 months	**8.9%** vs 1.4% after 180 days 12.4% vs 2% after 1 year 30% vs 3% after 3 years
FIND AF randomised	10-days ECG upon admission, after 3- & 6-months vs "standard"	402	73 ± 7 [≥60]	<7 months	**13.5%** vs 4.5% after 180 days 13.5% vs 6.1% after 1 year

(16.9%).[23] This difference was corroborated in EMBRACE,[24] CRYSTAL-AF,[25] and FIND-AF[26] (Table 2).

The STROKE-AF trial evaluated patients with stroke due to large- or small-vessel disease for AF with insertable cardiac monitors (ICM). There was a high diagnostic yield of 12.1% detection of occult AF over a 12-month period in patients with ICM vs 1.8% in the control group (HR, 7.4; 95% CI, 2.6–21.3; P<0.001).[27]

The PER DIEM trial compared external and internal monitoring with implantable loop recorders (ILRs). In the first 30 days, there were no differences in diagnostic yield, but in the longer term (12 months) ILRs detected AF lasting 2 minutes or longer in 15.3% of patients in the ILR group vs 4.7% of patients in the external loop recorder group (difference of 10.7% [95% CI, 4.0–17.3%]; risk ratio, 3.29 [95% CI, 1.45–7.42; P=.003]).[28]

In the MonDAFIS study, investigators tested whether 7-day continuous monitoring in the acute phase of stroke benefitted patients in the longer term as measured by OAC use after 12 months. Results revealed that systematic ECG monitoring had no effect on anticoagulant use at 12 months.[29]

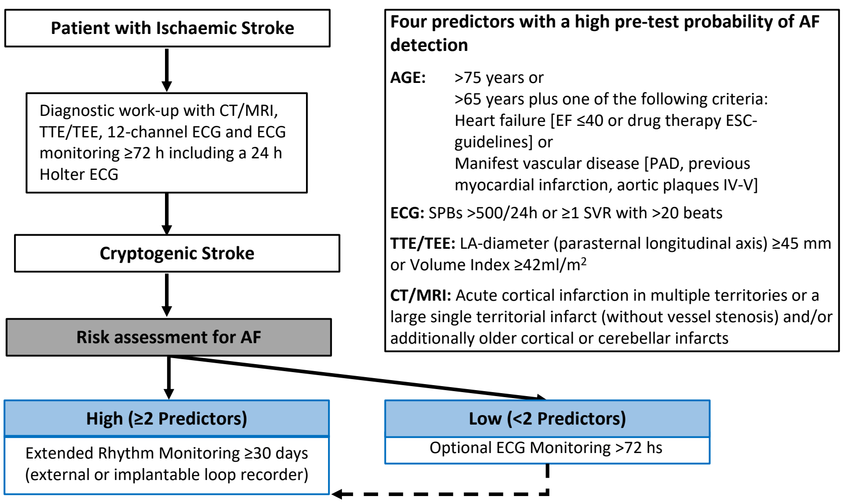
Predictors of paroxysmal AF

The most important clinical issue is not answered by the guidelines: the selection of the best candidates for long-term monitoring to improve resource utilisation. There are many predictors for occult AF based on ECG (supraventricular premature beats and short atrial runs),[30,31] echocardiography (left atrium diameter exceeding 45 mm),[32] and biomarkers.[33] Imaging studies such as MRI for plaque characterisation, and the ultrasound tests carotid Duplex and transcranial Doppler can detect microembolism.[34] However, age is the most significant AF predictor per CONFYRM-AF (HR per decade, 1.55; 95% CI, 1.11–2.15)[35] and CRYSTAL-AF (HR per decade, 2.0; 95% CI, 1.4–2.8; P=0.002).[36] Artificial intelligence can be useful too through the use of deep learning algorithms integrated into ECG to identify patients that could have occult AF.[37,38]

Pragmatic algorithm for selecting the right patients for long-term screening

Putting all the available information into practice may not be easy, and most stroke physicians make decisions on an individual basis after considering all the facts. The Austrian

Figure 2. Algorithm of predictors with high pre-test probability of AF detection.[39]



Stroke Society and Austrian Society of Cardiology defined a group of cryptogenic stroke patients with high pre-test probability of successful AF detection with long-term monitoring.[39] They found the four predictors detailed in Figure 2: if ≥2 are present, the patient should be monitored long-term; if one is present, it is an individual decision; and if none are present, it may not be worth performing long-term monitoring.

This scoring system has now been utilised for several years and it has helped to identify groups of high-risk patients with high diagnostic yield on long-term monitoring. However, although the components are evidence-based, it has not yet been fully validated. Retrospective validation based on single centre data indicated that occult AF can be detected in a large segment (50–60%) of patients who are identified by this algorithm. A long-term prospective validation study (ASUR) to refine cut-offs and inclusion of AI is ongoing and data will be available soon.

Unanswered issues and remaining challenges

There are still several challenging issues.

The first is what to do with a detected AF: patients with long episodes of AF should have anticoagulants, but a small proportion have very short AF episodes of only a few minutes, and it may be unclear whether these are related to higher stroke risk. It is expected that the ongoing studies, ARTESiA and NOAH-AFNET 6,[40,41] will provide more information once results are available.

The therapeutic management during the long-term screening phase remains challenging. Usually, treatment is prescribed once a diagnosis is made but in very high-risk patients it may be worth starting DOAC and long-term screening in parallel.

A recent study shows that screening AF in an older population results in less strokes in daily practice,[42] and new studies aim to corroborate this.[38,40,41] Other areas that should be investigated further are mechanistic aspects (epidemiology of post-stroke AF, advanced imaging, biomarkers and genetics, machine learning for detection and association) and patient selection (to determine when, how, and who should receive AF monitoring).

Conclusions

The first part of this symposium covered technological advances that can improve stroke care. The logistics of urgent stroke services include many stakeholders working in serial systems with abundant opportunities for delays. The AI software Viz.ai is an FDA approved technology that assists stroke teams through AI algorithms and a platform that facilitates communication.[4] There has also been progress in thrombectomy procedures as shown by the investigators at Vall d'Hebron Hospital regarding aspiration force and distensibility. These findings could help optimise thrombectomy strategies and aid the development of novel aspiration catheters.

The second part of the symposium covered clinical aspects of stroke care. Stroke has many causes but the cryptogenic type is a class where patient selection for monitoring and risk stratification are of paramount importance. Approximately 29% of cryptogenic stroke patients have occult AF which puts them at high risk of recurrent stroke and identifying them aids the implementation of secondary stroke prevention measures such as DOACs and LAAO. Extended monitoring with ILRs is superior to external devices at detecting AF and it may also be good to monitor segments of patients with stroke due to micro- or macro-angiopathy. A simple clinical decision algorithm can also assist clinicians in the diagnosis of occult AF.

Finally, cardiology and neurology services should collaborate closely and coexist under the wider umbrella of integrated management.

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