



# DRAWING CLOCKS HELPS TO DETECT BRAIN TOXICITY AFTER CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY

## PLAIN LANGUAGE SUMMARY

Source: Kazzi, C., Simpson, T., Wronski, M., Seery, N., Wesselingh, R., Tan, T. H., ... & Monif, M. CLOX and neurotox: Utility of the clock drawing task in monitoring for immune effector cell-associated neurotoxicity syndrome following chimeric antigen receptor T-cell therapy. British Journal of Haematology. 2025. <https://doi.org/10.1111/bjh.70044>

### WHY DID WE DO THIS WORK? WHY IS IT IMPORTANT?

- Chimeric antigen receptor T-cell (CAR-T) therapy is a newly approved treatment for many blood cancers. It is also being tested for other conditions.
- It is a therapy where a person’s own immune cells are processed in the lab so they can recognise and attack cancer cells. The engineered cells are injected back into the person.
- Chimeric antigen receptor T-cell therapy can be effective as a cancer treatment, but in some cases, it also has side effects.
- One of these side effects is toxicity in the brain.
- An early form of this brain toxicity can occur within the first two weeks after the cells are injected into the patient. This brain toxicity is called immune effector cell-associated neurotoxicity syndrome (ICANS).
- People can become confused and have difficulties with thinking, concentration, speaking, writing and remembering recent events.
- Brain toxicity can be mild or severe. Sometimes, it can be life-threatening.
- So, it is important to monitor for brain toxicity and treat it to prevent further damage.
- Doctors and nurses use a score known as the immune effector cell-associated encephalopathy or ICE score to help them monitor for brain toxicity. The score ranges from 0 to 10 and is determined from a brief set of questions (**Figure 1**).
- But research has shown that this ICE score can sometimes miss mild brain toxicity. For example, a person may have a perfect ICE score but still have underlying brain toxicity. Sometimes patients can lose points on the ICE score even if they do not have brain toxicity, but because of other reasons, like infection.
- So we need tools that can improve the ICE score for accurate diagnosis of brain toxicity.

**AlfredHealth**

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Unit:.....

**ICE NEUROLOGICAL ASSESSMENT**  
Immune effector cell-associated encephalopathy

Management of patients with acute Chimeric Antigen Receptor T cell (CAR-T) related neurotoxicity

UR

Family Name

Given Names

Address

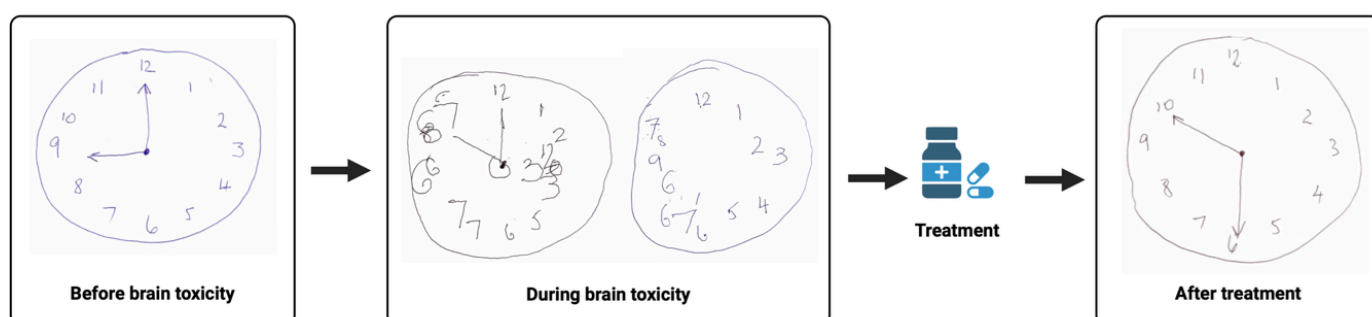
Date of Birth  Sex  Female  Male  Other

Start Date:												
Date / time	Year	Month	City	Hospital / Place	Follow command	Object 1	Object 2	Object 3	Serial 10s	Handwriting	Score	Grade
Staff initials	Sentence											

Figure 1. The ICE score.

## WHAT DID WE DO?

- Our team decided to use a test called the clock drawing task. In this two-minute test, patients are asked to draw a clock face and set the hands to a particular time as asked by a health professional. This test checks thinking and brain function using a 15-point scale.
- This study looked to see if the clock drawing task can be used in combination with the ICE score to improve the detection of brain toxicity after chimeric antigen receptor T-cell therapy.
- All patients who received chimeric antigen receptor T-cell therapy at the Alfred Hospital were asked to draw a clock at least once a day during their stay in the hospital.
- The first clock drawn by the patient was done before the T-cells were injected into them. This is called their 'baseline' clock. All the clocks drawn after their injection are compared to the baseline clock to see if the drawing is worse (**Figure 2**).
- Both the clock drawing test and the ICE scores can be done more frequently if a patient is suspected to be experiencing brain toxicity.
- We looked at the medical records of patients who had chimeric antigen receptor T-cell therapy between 2022 and 2024 at The Alfred Hospital.
- Two health professionals reviewed the medical records to collect data about brain toxicity, patient ICE scores, and clock drawings. All the clock drawings were scored out of 15.



**Figure 2.** A patient's clock drawings before brain toxicity, during brain toxicity, and after their brain toxicity has been treated. During brain toxicity, the patient cannot draw clock correctly.

## WHAT DID WE FIND?

- We scored 1212 clock drawings from 54 patients. Each clock was matched with an ICE score.
- We found 14 patients out of 54 had brain toxicity.
- Patients who developed brain toxicity drew poorer clocks compared to patients who did not develop brain toxicity.
- However some patients with brain toxicity could still draw clock faces correctly.

## WHAT DO THESE FINDINGS MEAN?

- The clock drawing task can be used by health professionals to complement the ICE score.
- It can assist health professionals to diagnose brain toxicity after chimeric antigen receptor T-cell (CAR-T) therapy.
- Health professionals should continue to use tools to detect brain toxicity after chimeric antigen receptor T-cell therapy as soon as possible.

## REFERENCES

- Reference for ICE score: Lee, D. W., Santomaso, B. D., Locke, F. L., Ghobadi, A., Turtle, C. J., Brudno, J. N., ... & Neelapu, S. S. (2019). ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. *Biology of blood and marrow transplantation*, 25(4), 625-638. <https://doi.org/10.1016/j.bbmt.2018.12.758>.
- Reference for original Clock Drawing 15-point score: Royall, D. R., Cordes, J. A., & Polk, M. (1998). CLOX: an executive clock drawing task. *Journal of Neurology, Neurosurgery & Psychiatry*, 64(5), 588-594. <https://doi.org/10.1136/jnnp.64.5.588>

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