BIS GUIDED TCI SEDATION
Refreshing the Blueprint for Procedural Sedation

Sedation is often described as a continuum, with all the attendant issues that such instability can produce.,

TCI provides you with the control and stability to position your patient where you wish on that continuum for the duration of the procedure.

I accept that many still believe that most sedation, and particularly pediatric sedation often end up as deep sedation.

Using the present blueprint for sedation, sedation can be difficult.

It is time to refresh the blueprint.

BIS-guided TCI can attain a level of safety and stability presently unattainable with traditional manual intermittent bolus drug delivery.

The goal of sedation is to administer a dose of a drug to achieve a specific clinical effect.

To achieve that specific clinical effect, we need a specific therapeutic concentration of that drug on the patient's receptors.

Optimal sedation is achieved by the maintenance of a steady-state concentration of drug being available at those receptors for the duration of the procedure.

TCI provides us with a stability of the drug brain concentration.

Stable brain concentrations enable accurate titration.

Present methods using a manual intermittent bolus technique with an agent such as midazolam, having a long TTPE (time to peak effect) now reckoned to be 10-13 minutes explains the frequent dose stacking and instability of such an outdated and inaccurate method of drug delivery.

It is difficult to maintain a steady state of suitable sedation by hand.

Historically in the search of a steady state of drug concentration operators turned to syringe driver infusion technology.

The effect of a syringe driver is to start with a bolus and then continue as a set rate constant infusion.

The problem is, is that the relationship between what is set as an infusion rate and the brain concentration is changing every second, and a plain syringe driver has no ability to account for that.

TCI or target controlled infusion, uses a syringe driver controlled by a pharmacokinetic algorithm for the drug being delivered to produce an accurate and stable brain concentration.

With TCI, we get an accurate bolus administration to reach the specified effect site (receptor) target concentration.

Accurate titration made by adjustment to the effect site target can rapidly enable the achievement of a safe and suitable level of sedation and then the TCI pump will maintain that same level for as long as is desired without continued manual intervention.

TCI achieves this steady state by reducing the time dependent variability of the infusion by continuously updating the infusion rate to consider the drugs characteristic to accumulate in the body.

TCI is described as using a BET scheme.
That is referring to BOLUS, ELIMINATION and TRANSFER
The pump calculates the initial bolus considering the patient's covariates that have been programmed into the pump, such as age, height, weight and gender.
The pump's pharmacokinetic modelling enables it to calculate continuously the drug lost from elimination or metabolism of the drug.
The model also continuously calculates the transfer and distribution of the drug between the peripheral compartments.
Pharmacokinetic behaviour can often be described by a three-compartment open model, with a redistribution phase followed by the elimination phase.

By giving values to the volumes of these compartments and the rate constants for the exchange of drug between compartments, and the drug's elimination, we can construct a formula, which allows us to calculate the concentrations obtained over time.

Once we know the concentration of the drug to produce the sedation effect, we need to establish the dose of the drug needed to obtain that concentration.

TCI is an infusion controlled in such a way as to achieve a user defined drug concentration in a body compartment or tissue of interest

You can think of TCI as using pharmacokinetics in reverse.

You choose the desired concentration on the receptors or effect site, and the computer calculates the administration rate using the pharmacokinetic model for the drug.

TCI is the logical solution to finding a safer more accurate method of administering drugs of sedation.

The drug models or algorithms supplied with TCI pumps are the Minto model for remifentanil and the Schnider model for propofol.
With effect-site targeting, the TCI system manipulates the plasma concentration to achieve the effect-site concentration as rapidly as possible.

When the effect-site target concentration is increased, the TCI system briefly increases the plasma concentration to an optimal level above the target effect-site concentration before temporarily stopping the infusion to allow the plasma concentration to decrease to the level of the chosen target effect-site concentration.

The systems use mathematical formulae to determine the magnitude of the optimal plasma concentration overshoot.

That is, the peak plasma concentration that generates a gradient sufficient to cause the most rapid increase in effect-

site concentration but without an overshoot of the effect-site concentration above your target.

If the target effect-site concentration is reduced the system stops the infusion, allowing the plasma concentrations to fall, thereby generating a concentration gradient out of the effect-site, until the estimated effect-site concentration has fallen to the new target.

At this stage, the plasma concentration will be less than the effect-site concentration, and so the system to maintain the target administers a small bolus to increase the plasma concentration to match the new target concentration.

TCI pumps maintain three superimposed infusions, one at a constant rate to replace drug elimination and two exponentially decreasing infusions to match drug removed from central compartment to other peripheral compartments of distribution.
So often people attempt to dismiss TCI by inferring that the algorithm can't be trusted as there is no blood sampling.
The TCI algorithm gets you to within 20% of the actual blood concentrations but that's acceptable. It is very like the vaporiser used with the volatile agents of general anaesthesia as they are of similar accuracy.
TCI gives you stable plasma and effect site concentrations, even if they are not 100% accurate as they are estimations it doesn't matter.
Titration to effect with stable concentrations is more accurate as stable concentrations are easier to titrate.
With a more stable concentration you can better assess dose response.
If the level of sedation is suitable, you can leave it and the concentration will remain stable.
If you wish to adjust effect up or down then it is easily and rapidly done.
TCI pumps consist of a user interface, a microprocessor and an infusion pump.

The microprocessor controls the graphic interface and enables the pharmacokinetic model for the drug on that pump.

It allows the input of patient data and instruction by the user.

It performs the necessary mathematical calculations, to control and monitor the infusion device.
The user programs the pump with the patient's data, being age weight, height and gender

The user enters a target drug concentration that they wish the pump to deliver at the effect site.

With TCI, the drug is now being administered by a device that has modeled at least 50% of that patient's variability into its drug delivery.

It is like a very smart syringe.

A Bi spectral index monitor is used to guide the sedation process

It is a neuro physiologic device that reads the EEG from the patient's frontal cortex and assigns a numerical value that broadly represents the depth of hypnosis for that patient.

BIS provides an objective way to measure a patient's level of hypnosis

BIS also provides information on the pharmacokinetic variability of the individual as well as the patient's drug tolerance and their response to stimulation during a procedure.

The system consists a sensor which attaches to the forehead of the patient and detects the EEG coming from the frontal cortex.

The BIS algorithm processes the raw EEG data derived from the sensor array by comparing it with its EEG database.

The index is a number between 100 and zero, where 100 indicates an alert and awake patient and zero would show a lack of EEG activity.

BIS is not an indicator of the level of consciousness

In a very general sense BIS levels for procedural sedation lie in the range of 65 to 85.

BIS can be variable, and you cannot count on it absolutely.

Some agents, such as remifentanil are poorly represented in the BIS.

Experience with BIS clarifies its shortcomings relating to such factors as neurologic disorders, certain medication, recreational drug use.

BIS monitoring is used as another parameter to aid titration.

The drugs used in BIS-guided TCI procedural sedation are propofol and remifentanil.

Propofol is the drug that most closely attains the requirements of what an ideal sedative drug should be. It has a rapid onset and a dose related sedative effect with anxiolysis and amnesia. It is antiemetic, has a rapid offset and provides a fast induction with an easy alteration to sedative level and a very crisp slightly euphoric recovery. It provides no analgesia and can cause a mean fall in arterial BP but at the levels of administration in sedation, the incidence of this change is low.
Remifentanil is the adjuvant of choice for the hypnotic propofol and acts as a hypnotic sparing agent.
Its synergism and different sedative properties improve the quality of the sedation. It too has a rapid onset which aids the ease of its titration by this method.
It provides very effective dose dependent analgesia and has an extremely rapid termination of effect independent of the time of its infusion rendering the need for an antagonist unnecessary.
TCI sedation commences with the pumps being programmed with the patient's covariates plus an initial effect site concentration target for each drug.
An effect site target concentration on startup of 1microgram per ml for propofol and 1 Nanogram per ml for remifentanil.
The pumps can be started concurrently or separately after observing peak effect for the individual drug.
The patient is observed as the initial boluses have an effect within 20-30 seconds.
Guided by voice communication and BIS we titrate towards a desired level of sedation.
Titration is achieved by selecting a higher (or lower) effect site target concentration and then waiting until the plasma level and the effect site level have equilibrated before making any further adjustments.

Once the desired level of sedation is reached, the pumps will then maintain that target concentration at the effect site for the duration of the procedure so producing a steady, stable, safe, predictable sedation that you can adjust on demand.

With the use of propofol and remifentanil we are targeting a percentage occupancy of different receptors.

Propofol targets the GABA receptors giving us sedation, amnesia, and euphoria, while for remifentanil it is the Mu opioid receptors giving us analgesia, euphoria and sedation.

The exact ideal ratio varies from patient to patient and from procedure to procedure.

In all sedation hypoxemia is the potential mechanism of injury, therefore, we have increased emphasis on monitoring ventilation v's saturation.

Therefore, the requirement is for accurate, real time monitoring for the possibility of an evolving hypercarbia.

Side stream capnography and supplemental oxygen is routinely employed.

Capnography provides early detection of respiratory change by monitoring exhaled CO2, essential as pulse oximetry is an insensitive and late phase monitor but does complement the capnography.

Other monitoring includes NIBP, BPM RR, and ECG if indicated.

TCI gives you the control to determine with some stability just where on the continuum of sedation you want to be.

TCI produces stable drug brain concentrations and provides the ability to manipulate these concentrations rapidly safely and accurately in a way that intermittent bolus techniques or infusions simply can’t.

The reality is that TCI uses more suitable drugs and TCI is the more logical and accurate method of administering those drugs.

It is the stability of the drug concentration attainable that is the most important aspect of safe sedation.

With a steady drug concentration titration to effect is more accurate, resulting in a safer sedative effect.

TCI enables safety, stability, control, and accuracy as well as predictability, flexibility, and a faster, and safer recovery.